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ROYAL SOCIETY.

REPORTS TO THE MALARIA COMMITTEE.

FIFTH SERIES.

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REPORTS, &c., FROM Messrs. STEPHENS AND CHRISTOPHERS, WEST COAST OF AFRICA.

"The Proposed Site for European Residences in the Freetown Hills." By J. W. W. Stephens, M.D. Cantab., and S. R. Christophers, M.B. Vict. Received November 26, 1900.

As a scheme for building European houses on the plateau above Freetown is under consideration, we, at the suggestion of Sir Frederick Cardew, K.C.M.G., investigated the neighbourhood of the proposed site. There are on these hills two straggling villages, Leicester and Gloucester, shown on the accompanying plan, but, apart from these, large areas are entirely free from habitations.

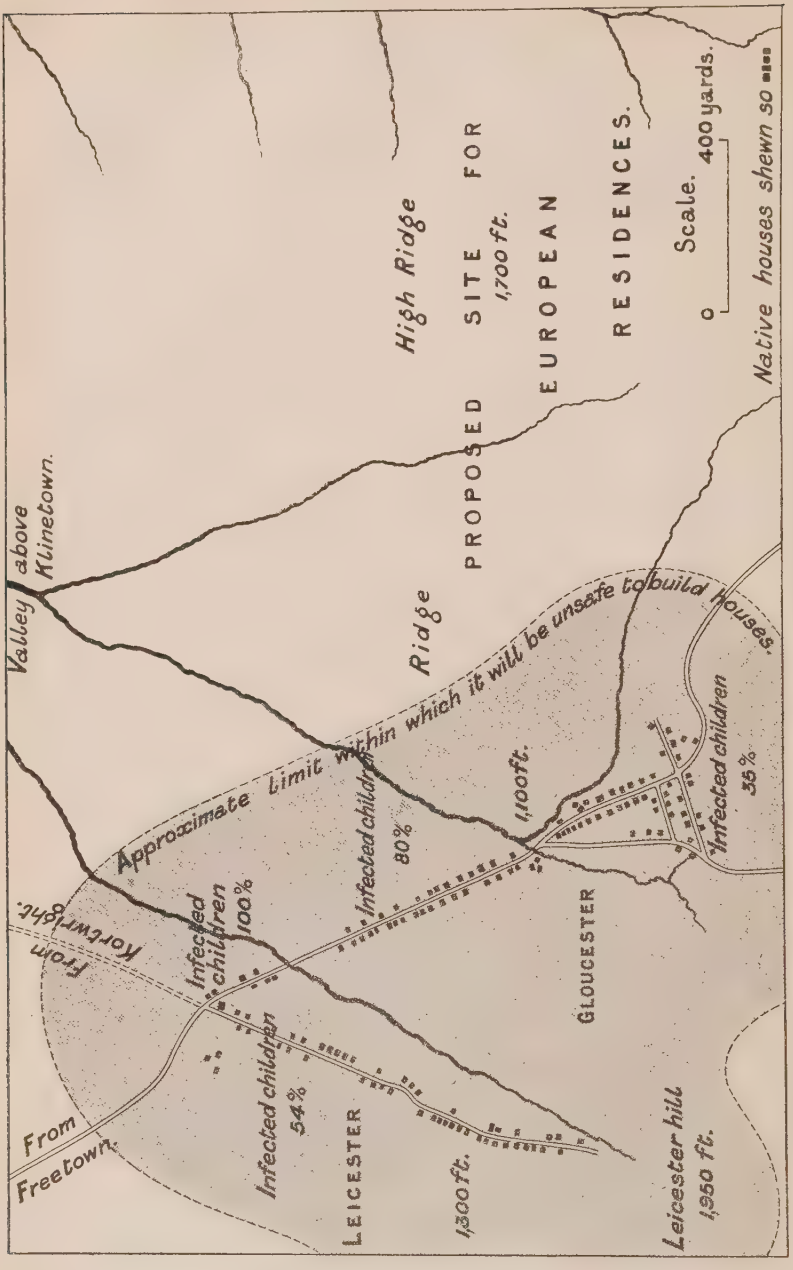
The children in Leicester and Gloucester show a considerable percentage of malarial infection, varying from 50 per cent. to 100 per cent. A portion of Gloucester, however, which is situated on a steep hillside, showed a diminished infection, namely, only 35 per cent. We believe the low figure observed in this part of Gloucester to be due to the extreme dryness of the hillside there, giving few opportunities for the existence of Anopheles, for elsewhere, as in Blantyre, at an elevation of 3000 feet, with numerous breeding grounds, malaria is rife.

There is, then, malaria on these highlands, and native quarters are here, as elsewhere, centres of malarial infection. Our surmise expressed in our first report on Freetown—that it would not be the elevation but the possibility of segregation which would make the scheme a success—was therefore correct.

We consider, then, that the proposed site—

(1) By reason of its remoteness from native dwellings;
(2) By reason of its dryness, if well chosen, giving few opportunities for Anopheles to breed;

will afford a complete freedom from malaria. It is essential, however, that native houses be rigidly excluded, and, as far as possible, native servants' quarters also. For we have seen elsewhere that even where breeding grounds are scarcely to be found, yet, under certain conditions, Anopheles, and these, moreover, infected, may occur.



Plan of portion of high ground above Freetown showing area to be avoided in choosing site for European houses.

It may be urged that we have overlooked the possibility of mosquitoes flying in from these villages, and as extraordinary statements

with regard to the flight of mosquitoes have lately appeared in print, it will not be out of place to record here our experience during nearly two years' residence in Africa in towns and in the bush under varying conditions:—

1. In Blantyre we occupied a house within 50 yards of Anopheles breeding grounds, and the house was naturally infested with Anopheles.

2. In a house 200 to 300 yards from the same breeding grounds we never observed any.

3. At Blantyre Hospital we never observed Anopheles, although breeding grounds were less than $\frac{1}{4}$ mile away.

4. In Freetown we have at different times occupied five houses, all less than $\frac{1}{4}$ mile, some much nearer, from innumerable breeding grounds, and in only one of these on one occasion did we observe Anopheles, and in that case the source was found in the neighbouring garden.

5. In Accra, in Bungalow 15, we never observed Anopheles, although plentiful less than $\frac{1}{2}$ mile away. Although in Accra it was stated that Anopheles flew in from a village 9 miles away, yet we found breeding grounds in profusion in Accra itself which completely explained their existence.

6. We have camped many nights a little distance ($\frac{1}{4}$ to $\frac{1}{2}$ mile) outside villages, and have not caught any Anopheles, though they were abundant in the villages.

These facts—and we could amplify them if necessary—must make it quite clear that Anopheles do not fly large distances, but remain in the neighbourhood of native huts, where they get a plentiful blood supply. From these they do often fly abroad, but it is at most a few hundred yards and not 15 miles.

Climatically, the change must be most beneficial. Even at an elevation of 700 feet (about half that of the proposed site) the atmosphere is fresh and even exhilarating, and one experiences the greatest relief after residence in Freetown with its most enervating foul atmosphere.

"The Increase in the Number of Large Mononuclear Leucocytes as a Diagnostic Sign of Malaria." By J. W. W. Stephens, M.D. Cantab., and S. R. Christophers, M.B. Vict. Received November 26, 1900.

In our first report ("Malarial and Blackwater Fevers of British Central Africa," p. 20) we noted the occurrence of an increase in the

proportion of the large mononuclear cells—also described by other authors in malaria.

We further showed the relation of this change to the temperature curve. That usually this change is absent during the pyretic periods, but very pronounced in the apyretic periods, or immediately following the rise of temperature, if only one such occurs. We also noted that in certain cases this change was extraordinarily marked, the large mononuclears during the apyretic periods even outnumbering the polynuclear elements. Also that in certain cases the change was to be detected even during the pyretic periods, but that in these it was always still further evident in the apyretic. In others that during the course of the fever no such change occurred, but that it appeared immediately the temperature subsided, rapidly diminishing again during convalescence.

We also pointed out that this change was of the greatest diagnostic importance in cases of malaria which had been treated by quinine, and in which, therefore, parasites were extremely scanty or absent in the peripheral blood.

A discussion on cases of malaria in which parasites do not appear in the peripheral blood occupies an accompanying report. In these the use of two diagnostic points is usually sufficient to enable one to be certain of their nature, apart from the actual presence of parasites. These two diagnostic points are (1) pigmented leucocytes, and (2) the mononuclear increase.

(1.) Pigmented leucocytes, even in severe malaria, are often very few and often require for their discovery prolonged search in large films. In two cases, although very few pigmented leucocytes were found after long search during life, yet the examination of the spleen post mortem showed large numbers of pigmented mononuclear leucocytes. In other cases, however, they are abundant.

(2.) Often in a case where pigmented leucocytes are difficult to find, a glance is sufficient to show that there is an excess of the large mononuclear elements. In order to obtain accurate results, 1000 leucocytes should be counted, but a count of three or four hundred is generally sufficient for diagnostic purposes, and the numbers so obtained do not differ much from the value of more extensive counts.

In counting the leucocytes, a well-made film is requisite The film is spread on a carefully-cleaned *slide* by means of the shaft of a large needle. A drop of blood is taken up by touching it with the slide near one end. The drop is made to flow along the needle by a slight to-and-fro motion parallel to the surface of the slide, and the needle is then, with an even movement, carried along the slide. By this means a large and thin film is obtained. The leucocytes are gathered for the most part in the borders and terminal points of the film, and can now readily be counted.

The mononuclear increase :—

a. We have shown, then, in malaria this is an almost constant occurrence.

b. Further, in native children, for the same reason, the mononuclear value is rarely normal. The majority show a percentage of 20 to 30 per cent., or even much greater.

c. Finally, we believe from the results obtained (*vide* report on Summary and Conclusions on Blackwater) by leucocytic counts of a considerable number of Europeans living in the tropics, that an increase beyond 15 per cent. is proof of an actual or recent malarial infection, and indeed, with a value over 20 per cent., it is often possible by long search to find a pigmented leucocyte, and a value as high as this probably implies actual infection at the time.

The diagnostic value of this increase in cases where no parasites are present is, then, of great importance.

"Malarial Fever without Parasites in the Peripheral Blood." By J. W. W. Stephens, M.D. Cantab., and S. R. Christophers, M.B. Vict. Received November 26, 1900.

From time to time in the examination of Europeans suspected of having malarial attacks, and who presented a rise of temperature with more or less constant vomiting, headache, pains in the bones, &c., we have been forced to conclude against the diagnosis of malaria, as no parasites were found, even after repeated examinations, or the number of parasites was so scanty as to cause doubt if they could be causally connected with the attack. We refer to cases in which no quinine had up to the time of the blood examination been given, for in the presence of quinine no such conclusion from a negative examination would be justifiable. How frequent these cases may be we have no means of estimating, and further, as a rule, there is no means of proving conclusively that such cases are malarial.

We give the following instances of which we have notes :

Case I. –J. Blantyre. Daily rises of temperature to about 100°. Then, after a few days, a tertian rise. Daily vomiting. It was only after prolonged examination for some days that a single ring-form parasite was found.

Case II.—S. Lagos. Well-marked subjective symptoms. Daily rises of temperature above 100°. Several blood examinations were made before any quinine had been taken. After prolonged search no

parasites were found. In a few days the temperature was normal. A leucocytic count now gave

Large mononuclears	24 per cent.
Small „	10 „
Polymorphonuclears.....	66 „

but no pigment was found. We felt certain that this was a case of malaria, and a re-examination of the blood taken, before quinine, now revealed, after again long search, one parasite, confirming thus the diagnosis based entirely on the leucocytic count.

Case III.—The following is a case where clinically there was not the slightest doubt as to the malarial nature of the attack, but there was absolutely no proof objectively.

C. Sierra Leone.

28.10.00. Evening temperature, 99·4°. Feeling unwell.

29.10.00. 5 P.M. Temp. 103°. Much vomiting. Blood examination negative. Quinine, 1·0 gramme. Mostly vomited.

30.10.00. 6 P.M. Temp. 100°. Vomiting continually. Blood examination negative. Quinine hypodermically.

		29th, 5 P.M.	30th, 8 A.M.	30th, 6 P.M.
Leucocytes :	Large mononuclears ...	16·4	15·2	15
	Small „ ...	7	11·2	14
	Polymorphonuclears ...	76·6	73·6	71

The two cases of malaria produced experimentally in England by Anopheles brought from Italy, reported by Dr. Manson and Mr. Rees, also show this condition.

Case IV.*—P. M. Bitten by infected Anopheles. 29 and 31.8.00. Also on 2 and 4.9.00. Also 10 and 12.9.00.

13.9.00. 9 A.M. t. 99°. 4.30 P.M. t. 101·4°. Headache, lassitude, chilliness, pains in the back and loins. Repeated blood examinations negative.

14.9.00. t. ranged between 101° and 102°. Subjective symptoms exaggerated. No parasites.

15.9.00. 7 A.M. t. 100·4°. No parasites.
4 P.M. t. 103·6° Delirium. No parasites

16.9.00. 8 A.M. t. 98·4 One doubtful parasite.
7 P.M. t. 102·8°.

17.9.00. 10 A.M. t. 99°. Several parasites. Two pigmented leucocytes. Later many tertian parasites.

* "Experimental Proof of Mosquito Malaria Theory," Manson, 'Brit. Med. Journ.,' September 29, 1900, p. 950.

Had quinine been given on the 14th or 15th there can be no doubt that subsequent examinations would likewise have revealed no parasites.

Case V.—G. W.* Fed infected mosquitoes on his blood (? 14.8.00).

28.8.00. Feeling ill. 5 P.M. t. 101·6°. No parasites.
29.8.00. One pigmented leucocyte.
30.8.00. Four pigmented leucocytes.
1.9.00. 8 P.M. t. 101°. No parasites.
2.9.00. 9 P.M. t. 102°. Midnight, 104·4° No parasites.
3.9.00. Morning. Parasites.

The two cases illustrate the fact that a high temperature may occur for some days without the existence of parasites in the blood. For the purposes of the experiment quinine was not given until the diagnosis had been established. Had quinine been given early, as universally in practice is the case, there would have been no evidence of the existence of parasites in either of these cases. They are, then, of particular value as showing that *a high temperature persisting for some days is not necessarily accompanied by parasites*, so that the absence of parasites does not necessarily exclude a malarial infection.

We think that such cases as these are by no means isolated, and although, broadly speaking, it is true that there is no malaria without parasites in the peripheral blood, yet exceptional cases make it extremely important for diagnostic reasons that some other means (*e.g.*, a serum reaction) for the diagnosis of malaria be discovered.

Another class of cases in which the clinical symptoms of malaria are often pronounced, though no parasites occur in the peripheral blood, is seen after the taking of quinine in the course of an ordinary attack.

The following cases show how a high temperature may persist for some days, but, nevertheless, no parasites be found. In these cases parasites were detected before quinine had been taken, but more commonly the patient is not seen until after the administration of quinine, and then so far as parasites are concerned the examination is negative.

Case VI. C. 11.10.00. t. 102°. Numerous parasites.

Leucocytes	Large mononuclear ...	8·6 per cent.
	Small „ ...	6·6 „
	Polynuclear	84·8 „

12.10.00. Thirty-six grains quinine since last examination. No parasites. No pigment.

* "Experimental Proof of Mosquito Malaria Theory," Rees, 'Brit. Med. Journ.,' October 6, 1900, p. 1055.

13–17.10.00. Thirty grains of quinine daily. High temp. No parasites.

18.10.00. First day of normal temperature.

No parasites. No pigment.

Leucocytes { Large mononuclear ... 30 per cent.
Small „ ... 15 „
Polynuclear ..... 55 „

Showing a well-marked mononuclear increase.

Case VII. M. 12.3.99. t. 104·8°. Parasites. Mononuclear increase.

13.3.99. t. 102·4°. Parasites. Mononuclear increase. Quinine.

14.3.99. t. 101°. Parasites scanty. Mononuclear increase. Quinine.

15.3.99. t. 101°. No parasites. Mononuclear increase. Quinine.

16.3.99. t. 101°. No parasites. Mononuclear increase. Quinine.

17.3.99. t. 100·4°. No parasites. Mononuclear increase. Quinine.

18.3.99. t. 99°. No parasites. Mononuclear increase. Quinine.

The bearing of the examples given above on the argument usually adduced to prove that blackwater is non-malarial, viz., that parasites are absent or in quite insufficient amount to account for the symptoms, is obvious. The argument fails; a complete absence of parasites in all cases of blackwater would not necessarily exclude malaria. Further, we believe that in a different class of cases, viz., those suffering from constant attacks of fever, who yet at the same time are more or less constantly taking quinine, parasites are frequently absent.

"The Tonicity of the Blood in Malaria and Blackwater Fever." By J. W. W. Stephens, M.D. Cantab., and S. R. Christophers, M.B. Vict. Received November 26, 1900.

In our report on the "Distribution of Anopheles" in Sierra Leone, pp. 64 and 73, we appended some observations on the tonicity of the blood in malaria and blackwater fever. The method used was rough, and it was difficult to express accurately in words differences which, however, were quite well appreciated by the eye, and which could be best

expressed by some colorimetric method. Lesage,* using such a method, expresses his data in the form of a curve, and the results are more striking and easily followed. As we had no convenient means of estimating the hæmoglobin set free by the various solutions used, the following method was devised as being an improvement on that previously used, and capable of fairly accurate expression in numerical values, which could if necessary be represented in the form of a curve.

The stem of the ordinary Thoma-Zeiss pipette is divided into ten divisions. The drop of blood used for making the observation of tonicity was that contained in two of these divisions, so that five observations could be made simultaneously with the same specimen of blood taken from the patient's finger.

Four salt solutions were used, viz., 0·41, 0·39, 0·37, 0·35 per cent. In a control experiment, then, two divisions of the blood in the pipette were added to 1 c.c. of each solution in a small test tube. The last two divisions were added to 1 c.c. of water. Complete hæmolysis, of course, takes place in this solution. The colour given by this was for convenience' sake called 100 per cent. Solutions were also prepared in water, and this can be readily done, for purposes of comparison in which the amount of hæmoglobin was 90, 80, 70 per cent., etc., to 10 per cent. So that we had a series of standards with which the colour in the respective tubes containing salt could be compared.

These standards have the advantage of being solutions of Hgb., like that resulting from hæmolysis. They have the great disadvantage that they are not permanent.

In making an observation of tonicity, 1 c.c. of each of the four salt solutions was used, and the fifth tube contained water. The colour of this tube being now compared with that of the controls, the amount of Hgb. could be readily determined in terms of the standard control. A correction for differences in the amount of Hgb. in the tube containing water is necessary, otherwise a low reading may give a false view of the amount of hæmolysis, which may actually be greater than the control in a case where it is apparently less. On the other hand, the amount of hæmolysis in a malarial patient, is really less than it should be if no correction is made for anæmia.

Examples of the tonicities in malaria and blackwater fever are:

	0·41 per cent. salt.	0·39 per cent.	0·37 per cent.	0·35 per cent.	H_2O.
I. Malaria, 1...	25	40	60	—	—
II. „ 2...	40	65	80	90	90
III. Control.....	0	20	65	90	100
IV. Blackwater..	0	0	0	20	—

* Lesage, 'Comptes Rendus Hebdomadaires de la Soc. de Biol.,' Juillet 28, 1900, p. 719.

The observations on the tonicity in malaria are quite in accord with those we have previously recorded.

In the blackwater case we did not at the time observe the value with water, but the anæmia was quite insufficient to account for the low tonicity which we have observed also in three other cases; in the remaining cases it was the same as the control or slightly raised.

We may summarise here these and our previous observations.

1. In malaria we have constantly observed a high tonicity.
2. In blackwater there is occasionally a remarkably low tonicity, in other cases it has the normal value or somewhat raised value as in malaria. The low or normal value in blackwater may be due as we have previously suggested to the fact that the weak corpuscles—those of high tonicity—are destroyed, or it may be due to the fact that the tonicity of the corpuscles, as a whole, is changed after the liberation of hæmoglobin. If hæmoglobinæmia is present (and we have only observed it in two cases) it however will not materially interfere with the reading of the values, as the amount due to this cause can also be determined in a hyper-tonic solution.

The presence again of a yellow serum may cause difficulty.

We may add to these conclusions a third derived from a series of observations on native blood.

3. The tonicity of native blood is often remarkably low: a low value not observed by us in any European blood.

The difference may be as great as 0·04 to 0·06 per cent. salt.

"Blackwater Fever. Cases IX to XVI. Summary and Conclusion." By J. W. W. Stephens, M.D. Cantab., and S. R. Christophers, M.B. Vict. Received November 26, 1900.

I. Record of Cases.

Case IX.—M. Sierra Leone. Blackwater many times previously. Had fever three weeks before present attack, was taking quinine, still feeling unwell continually.

21.3.00. 3 A.M. shivering attack. 6 A.M. t. 100°. Quinine, 1·0 gramme.

22.3.00. 6 A.M. t. normal. Quinine, 0·6 gramme. 5 P.M. t. 101°. Quinine, 0·6 gramme.

23.3.00. 6 A.M. t. normal. Quinine, 0·6 gramme. 10 A.M. rigor. 12.30 P.M. Blackwater. 7 P.M. urine contained hæmoglobin, but not in large amount. Urobilin present.

25.3.00. Urine. No. Hgb. Urobilin present.

Blood examinations :

23.3.00. No parasites. Several leucocytes have fine grains of pigment. A few have golden yellow pigment.

Leucocytes :

17.3.00	Large mononuclear...	22·9	per cent.
	Small „ ...	2·7	„
	Polynuclear.....	73·4	„
23.3.00	Large mononuclear...	17	per cent.
	Small „ ...	3	„
	Polynuclear.....	70	„
24.3.00	Large mononuclear...	23·6	„
	Small „ ...	6	„
	Polynuclear.....	68·6	„
25.3.00	Large mononuclear...	19·3	„
	Small „ ...	14·7	„
	Polynuclear.....	65·1	„
26.3.00	Large mononuclear...	15·2	„
	Small „ ...	8	„
	Polynuclear.....	76·7	„

Case X.—T. Sierra Leone.

31.3.00. In evening vomited after food ; later took quinine, 0·6 gramme.

1.4.00. Early morning (before 6 A.M.). Blackwater.
Urine. Oxyhæmoglobin. Urobilin absent.
Blood. No parasites. Two pigmented mononuclear leucocytes.

Leucocytes :

10 A.M.	Large mononuclear...	18·75	per cent.
	Small „ ...	11·4	„
	Polynuclear.....	69·85	„
3 P.M.	Large mononuclear...	27	„
	Small „ ...	19	„
	Polynuclear.....	54	„

4 P.M. Hæmoglobinæmia.

2.4.00. 8 A.M. 0·5 gramme quinine hypodermically. 2 P.M. vomiting. 3 P.M. urine, methæmoglobin. No urobilin. t 98°.

No further examinations made. Death. No autopsy.

Case XI.—E. Lagos. 2½ years in Soudan, 20 months in Lagos.

Much fever during first year and on voyage home. Does not use a mosquito net.

11.7.00. Feeling unwell in morning. 8 A.M. quinine, 0·6 gramme. Got wet through during day. 8 P.M. quinine, 0·6 gramme. 9 P.M. passed a dark urine. No hæmoglobin; no urobilin; no bile pigment.

12.7.00. 4 A.M. darker urine. Methæmoglobin and oxyhæmoglobin (slight). Spleen palpable. Earthy pigmented (jaundiced) condition of skin.

13.7.00. Hæmoglobin well marked.

14.7.00. Hæmoglobin, very weak bands.

Blood examinations:

12.7.00. Parasites. Pigmented leucocytes.

Leucocytes	Large mononuclear ...	21·5	per cent.
	Small „ ...	16·4	„
	Polynuclear	61	„

13.7.00. No parasites. Pigmented leucocytes.

Leucocytes	Large mononuclear ...	11·5	per cent.
	Small „ ...	12	„
	Polynuclear	75	„

Blood serum rather yellow.

Hæmoglobinæmia doubtful.

Tonicity of blood identical with that of a normal control.

Recovery.

Case XII.—D. Lagos. Blackwater two or three times previously. "Influenza" attack when last home.

17.7.00. Feeling unwell. Temp. raised. Took quinine, two or three 2-grain tabloids. Worse in evening (? more quinine). Rigor in night.

18.7.00. Rigor. Blackwater. Methæmoglobin. No urobilin. Blood. No parasites. No pigment.

Leucocytes	Large mononuclear ...	6·4	per cent.
	Small „ ...	4·5	„
	Polynuclear	89	„

19.7.00. Death. No autopsy.

Case XIII.—A. Lagos. 3rd attack of blackwater, last, 1 year 9 months ago. Suffering from slight fever attacks previous to present attack.

10.8.00. Pigmented leucocyte.
18.9.00. Quinine, 0·3 gramme.
19.8.00. 6 P.M. Quinine, 0·3 gramme.
10 P.M. Blackwater.
20.8.00. 7 A.M. t. 103°. Urine. Methæmoglobin. No urobilin. No bile pigment.
5 P.M. t. 103·4°. Jaundice.

Blood examinations:
20.8.00. 7 A.M. No parasites. No pigment.

Leucocytes	Large mononuclear ...	21·5	per cent.
	Small „ ...	13·5	„
	Polynuclear	65	„

Hæmaglobinæmia. Tonicity slightly raised.
5 P.M. Typical pigmented mononuclear leucocyte.

Leucocytes	Large mononuclear ...	21·6	per cent.
	Small „ ...	17	„
	Polynuclear	61·3	„

21.8.00. 5 P.M. t. 102°.

Leucocytes	Large mononuclear ...	18·5	per cent.
	Small „ ...	17	„
	Polynuclear	65·5	„

Death, midnight. No autopsy.

Case XIV.—B. Lagos. Much fever recently. Taking a quinine mixture for last few days (about 0·3 gramme daily).
19.9.00. 5 P.M. t. 102°. 9.45 P.M. blackwater. Quinine, 0·6 gramme (quinine probably after blackwater, but doubtful when). Methæmoglobin. 12 P.M. 0·3 gramme quinine.
20.9.00. 4 A.M. Rigor. t. 106·2°. 2 P.M. no Hgb. No urobilin.

Blood examinations: Extreme anæmia. 10–20 per cent. Hgb. No parasites. No pigment.

Leucocytes	Large mononuclear ...	23	per cent.
	Small „ ...	23	„
	Polynuclear	54	„

Tonicity slightly lowered or normal. Determination very difficult owing to extreme anæmia.

Case XV.—C. s.s. "Sobo." Blackwater in June. Invalided home. Fever on board ship.

27.9.00. Quinine, 0·6—1 gramme. Blackwater some hours after in the evening.

28.9.00. Blood examinations: No parasites. No pigment.

Leucocytes	Large mononuclear...	24·8	per cent.
	Small „ ...	13·6	„
	Polynuclear.....	61·5	„

Case XVI.—Cl. Sierra Leone.

4.10.00. Vomiting.

5.10.00. Went to bed. Quinine, 0·6 gramme in evening.

6.10.00. 6 A.M. Quinine, 1·0 gramme. Blackwater.
9 A.M. Quinine, 1·0 gramme.
9 P.M. Urine with small amount of hæmoglobin only.

Blood examinations: No parasites. 2 pigmented mononuclear leucocytes. 1 pigmented polynuclear leucocyte.

Leucocytes	Large mononuclear...	11·6	per cent.
	Small „ ...	12	„
	Polynuclear.....	75·5	„

7.10.00. Urine. Trace only of Hgb.

Leucocytes	Large mononuclear...	15·5	per cent.
	Small „ ...	10	„
	Polynuclear.....	74	„

II. Summary.

I. *Relation of Blackwater to Malaria Tropica.*—While it is true that malaria may be very prevalent in a country with little or no blackwater, yet, on the other hand, blackwater fever has never been shown to exist in the absence of malaria, and, on the contrary, it can hardly be a matter of coincidence that in those countries where malaria fever is most malignant, there also blackwater is a scourge.

Further, it is characteristic of their co-existence that the type of malarial fever is the æstivo-autumnal (malignant tertian), or tropical parasite, although very occasionally blackwater and mild tertians have been found together. Thus, in those regions of Africa where malaria and blackwater co-exist, we have the following figures:—

German East Africa ...	89 per cent. malarial cases = tropical parasite (Koch).
British Central Africa...	100 per cent. malaria cases = tropical parasite (Malaria Commission).

Sierra Leone ..... 100 per cent. malaria cases = tropical parasite (Malaria Commission).
Gold Coast ..... 100 per cent. malaria cases = tropical parasite (Malaria Commission).
Lagos ..... 100 per cent. malaria cases = tropical parasite (Malaria Commission).

Further, there is this difference between the malarial fever (æstivo-autumnal) of Italy and that of tropical zones of Africa, that in the latter malaria *prevails throughout the year* without any seasonal intermission. It may be true that malaria is more prevalent in the tropics in the intermediate times between the rains and dry season, but on this point there seems to be a considerable difference of opinion. Statistics are by no means convincing, as at all times many cases of fever are not recorded at all. Yet, whenever we have examined Anopheles from native huts, even in the middle of the dry season, we have found no appreciable difference in the number infected, and so Europeans are subject to a constant all-the-year-round infection. As a matter of fact, if we take a number of Europeans, as on a railway, we find that they are more or less constantly suffering from slight fevers, which show no seasonal prevalence. There is, then, no definite intermission in the danger of infection, and this fact, viz., constantly occurring infection, constitutes an important difference from the fevers of temperate climates, where, in the winter, there is a marked decline in infection.

It has been stated that the seasonal prevalence of blackwater bears no relation to that of malaria. And, in fact, statistics have actually been published based upon an indiscriminate compilation of native and European cases, none of which were examined microscopically. If we consider alone the doubtfulness of so-called "fever" in adult natives, such statistics are quite valueless, and it is futile to discuss seriously arguments based thereon as to the seasonal prevalence of malaria and blackwater. Speaking broadly, in most places in tropical Africa there is no very definite seasonal prevalence of either malaria or blackwater.

II. *Premonitory Symptoms in Blackwater.*

In a very large proportion of blackwater cases the patient has for two or three days previously had considerable rises of temperature with vomiting and other symptoms. This initial illness is rarely seen by the medical man, nor are blood examinations made at this time, so that the nature of the illness is often obscure. The character of the temperature curve, however, when obtained, and the almost invariable presence of parasites when a blood examination is made prior to the blackwater, render it very probable that the initial illness which so

commonly occurs before the taking of quinine is *malaria*. Were blackwater to depend alone upon the taking of quinine, one would not expect to find this initial illness so constant a phenomenon.

III. *The Absence of Malarial Parasites in Blackwater.*

A common feature in blackwater cases which are not seen very early is that there is a complete absence of parasites. This is evident from Table I, where in only one case were there parasites present during the blackwater.

If blackwater is a process independent of malaria, then we should expect in those cases where parasites were present that they would follow their usual cycle of development with characteristic temperature curve, superadded to that due, *ex hypothesi*, to the blackwater. But this is contrary to our own experience and that of all observers who have examined the blood microscopically.

Parasites disappear, and do so rapidly: as there is almost always without exception a history of quinine, we think that this will to a large extent account for their disappearance. If we were dealing with an equivalent number of cases of malaria instead of blackwater, as we have shown in an accompanying report, the percentage of cases in which parasites would be found subsequent to the taking of quinine, would be remarkably low. Quinine alone would quite well account for the fact that parasites are so rarely found in blackwater. Whether any other factor is responsible we have no means of saying.

We have previously quoted cases where, although malarial parasites were absent at the time of the blackwater, yet later, under conditions which excluded the possibility of a fresh infection, parasites have reappeared, showing the presence of a malarial infection which at the time of the blackwater was not evident. We had at the time overlooked several instances of this kind recorded by A. Plehn* and F. Plehn.† They are sufficiently important, we consider, to justify us in calling attention to them here.

Examples of Cases where Parasites originally present disappear with the Onset of Blackwater, or, where originally absent, they have appeared later.

1.	4.9.	Fever. *Scanty parasites.*
	5.9.	Quinine, 1·0 gramme. 2 hours later blackwater. *No parasites.*
	16.9.	Weak and feverish. *Parasites.*

* 'Berträge zur Kentniss von Verlauf und Behandlung der Tropischen Malaria in Kamerun.'

† 'Die Kamerun Küste.'

	17.9.	12 midnight, shivering. 1 A.M., blackwater (? quinine previously).
2.	13.11.	Morning, quinine, 1·0 gramme. 12 noon, rigor. 4.30 P.M., blackwater.
	14.11.	A *single parasite* found.
	22.11.	Numerous parasites.
3.	4.10.	Occasional *parasites.*
	5.10.	Morning, quinine, 1·0 gramme. 12 noon, blackwater.
	6.10.	*No parasites.*
4.	3.9.93.	9 A.M., slight fever. Quinine. Rigor. Blackwater. *Numerous parasites.*
	4.9.93.	Urine clear. 8 A.M., t. 103°. Vomiting. Blackwater. *No parasites.*
	5.9.93.	Convalescent.
	19.9.93.	Slight fever.
	20.9.93.	6 A.M., quinine, 1·0 gramme. 9 A.M., rigor. 10·45 A.M., urine, no Hgb. 12 noon, urine, Hgb. *Numerous parasites.*
	21.9.93.	*No parasites.*
	9.10.93.	Fever.
	10.10.93.	7 A.M. Quinine, 1·5 grammes. 9 A.M. Rigor and blackwater. *Parasites scanty.*
5.	13.11.94.	Many crescents and *parasites.* Quinine, 1·0 gramme. 1 hour later. Rigor and blackwater.
	16.11.94.	*No parasites.*
6.	6.6.84.	Slight fever.
	7.6.94.	6 A.M. Quinine, 1·5 grammes. 8 A.M. Rigor. Blackwater. *Numerous parasites.*
	8.6.94.	Urine clear. 12 noon. t. 102°. Blackwater.
	9.6.94.	No parasites.

In an accompanying report (p. 7) we have shown how commonly ordinary malarial infections, more especially when quinine has been taken, fail to show any parasites. We thus have in undoubted malaria a parallel condition to that in blackwater.

IV. *Relation to Quinine.*

A consideration of the cases recorded by Tomaselli (the first was recorded forty years ago), by Karamitsas, by the Roman school (Marchiafava, Celli, Bignami), by A. Plehn and F. Plehn, and lately by Koch, make it perfectly clear that quinine can under certain conditions induce hæmoglobinuria, and that there are no reasons for believing that tropical hæmoglobinuria (blackwater) in any way differs from the quinine hæmoglobinuria of Europe.

One of Tomaselli's cases :—*

August, 1860. First attack of malaria. Cured by quinine.

1. A month later. A relapse. 1 gramme of quinine. Some hours later—rigor, high fever, vomiting, hæmaturia, and icterus (*blackwater*).
2. During remissions of the fever a larger dose of quinine was again given per rectum owing to the vomiting. The result was as before only more intense (*blackwater*).

   No more quinine was given. Recovery took place in a few days.
3. A month later. Mild fever. A decoction of quinine well borne, but the fever being intense on repeating the dose the result was very different. About 5 hours after the quinine, rigors, hæmaturia, vomiting, icterus (*blackwater*).

   The fever lasted 18 hours. Then defervescence.
4. Fifteen days later. A relapse. 1 gramme quinine sulphate per rectum. 4 hours later—tremors, vomiting, bloody urine, icterus (*blackwater*). Recovery. 2 months of good health.
5. 21st April. Fever with rigor; vomiting. 23rd. A still more grave paroxysm, so that it was thought necessary to again try quinine. Antimoniate of quinine in decigramme doses every 2 hours. The first dose was given precisely when the malarial paroxysm began to remit. Hardly 2 hours after the first dose had been given there set in rigors, vomiting, hæmaturia, &c. (*blackwater*).
6. 25th April. A fourth febrile paroxysm. Urine now clear. Fearing the fatal effects of a return of another paroxysm, quinine was, in consultation, again ordered as soon as the remission commenced. 50 centigrammes of the bisulphate in a clyster were given 6 A.M. on the 26th. Two hours later the usual train of symptoms—hæmaturia, icterus (*blackwater*), death.

One of Koch's cases :—†

Patient four years in Cameroons. Had blackwater seven times, always following quinine. Patient now in Berlin. From time to time slight fever attacks.

Got wet. Rigor. t. 40·6°. Took two doses of quinine, 0·2 gramme.

Next day, blood examination negative.

* 'La intossicazione chinica e l'infezione malarica' (Comm. Salvatore Tomaselli).

† Koch, 'Über Schwarzwasserfieber (Hæmoglobinurie),' s. 316.

Some weeks later, fever attack. By instruction had taken no quinine. Blood examination positive. (Large pigmented tertians.)

Patient advised to take methylene blue and no quinine, but after a few days he consulted another physician, who ordered him quinine.

Scarcely had he taken the quinine when a violent attack of *blackwater* ensued. Brought into hospital.

2nd. (4 × 0·1) gramme quinine—a few hours—*blackwater*. t. 40·5°. No parasites.

6th. (4 × 0·1) gramme quinine—a few hours—*blackwater*. t. 41·0 . No parasites.

14th. (4 × 0·1) gramme quinine—a few hours—*blackwater*. t. 39·5 . No parasites.

24th. (4 × 0·1) gramme quinine—a few hours—*blackwater*. t. 41·5°. No parasites.

It would appear from the criticisms made on Koch by many writers that they have not taken the trouble to acquaint themselves at first hand with his writings, for views are constantly attributed to him which certainly are not to be found in his writings; and, further, there seems to be a general impression, at least among English writers, that Koch was the first and only person to enunciate the quinine hypothesis. Such an impression, a knowledge of the literature of blackwater would have removed. A study of 200 cases published by competent observers, and our own cases, has convinced us of the causal connection between quinine and blackwater.

Among our own cases we have not met with one in which quinine could be excluded beyond all doubt, but, on the contrary, the blackwater followed more or less closely after the quinine.

Why quinine at one time can produce blackwater and a few hours or days later not, it is impossible in the present state of our knowledge to say. We can only expect that a solution will be forthcoming when toxic hæmoglobinurias generally are more closely investigated, and when some new light is thrown upon such an obscure disease as the paroxysmal hæmoglobinuria of temperate climates.

V. *Evidence of Malaria in Blackwater.*

We have previously seen that, in a large proportion of cases of blackwater, parasites are not to be found by the most careful search. This, indeed, has led some authors to conclude that many cases of blackwater occur without any accompanying or closely-preceding malarial infection.

A study of cases, however, of undoubted malaria in which quinine

has been administered leads us to consider that parasites in the peripheral blood are not necessarily present even in undoubted cases of malaria, and that their absence in blackwater may be quite compatible with a severe malarial infection. We therefore examined the blood in our cases of blackwater with a view to determine whether or no they showed the less striking evidences of malaria such as we still find in ordinary cases of malaria treated by quinine, *i.e.*, the presence of pigmented leucocytes and an increase in the large mononuclear leucocytes. We have pointed out elsewhere that in cases where the autopsy revealed severe malarial infection, pigmented leucocytes have been extremely rare in the peripheral blood, and that it is often only at certain times that the increase in large mononuclear leucocytes is to be detected. We do not, then, expect in every case of malaria to find pigmented leucocytes in abundance, or to find without repeated examination a marked leucocytic variation. In blackwater, also, if it is malarial in nature, we should not expect in every case gross evidence of malarial infection, more especially as blackwater for the most part occurs in those who have been some years in the tropics and who suffer from modified attacks of malaria rather than severe attacks.

In the accompanying table (p. 24) a tabular arrangement of our sixteen cases of blackwater is given showing the evidence of malarial infection at the time of the attack or immediately prior to it. It will be seen that in one case (Case 3) blackwater came on in the course of an ordinary severe attack of malaria, that with the onset of blackwater there was a coincident disappearance of parasites. In Case 11, which was seen earlier in the disease than usual, parasites were at first present, but later disappeared. In Cases 2, 4, 5, 8, 9, 10, 13, 16, at least one typical crowded pigmented leucocyte was found, and in several cases these were common. In Cases 14, 15, 17, although neither parasites nor pigmented leucocytes were seen, yet the number of large mononuclear leucocytes was in every case over 20 per cent., a percentage which we have in Table II shown is very strong evidence of malarial infection. One case only (Case 12) has failed to yield evidence of malarial infection, and in this case our investigation was confined to a single blood examination and hampered by the fact that the only films available were badly made. In Case 1 fresh films only were examined, and as pigmented leucocytes were not especially searched for, and as the leucocytes were not counted, we have omitted it from the list.

In 16 cases of blackwater we have, then, evidence of malarial infection in 15, *i.e.*, in 93·8 per cent. As in Koch's cases, parasites themselves were found in over 40 per cent., we think it highly probable that, had attention been paid to pigmented leucocytes and the proportion of leucocytes, his cases would have shown an equally high percentage of malarial infection. Two post-mortems in which no

pigment was found are certainly against this view, but we would point out that in a case of blackwater described by Dr. Thin, although there was only extremely scanty pigment in the spleen, yet there were sporulating parasites in the brain; also that in these cases of Koch death occurred on the 5th and 10th day respectively after the onset of the blackwater, possibly long enough for the pigment from a mild attack to disappear. In five post-mortems of our own we have found abundant pigment occurring in such a way as to make it certain that it arose from very recent attacks coincident with the onset of the blackwater. As no parasites were found (except in one case where numbers of developing gametes were found) it would appear that the disappearance of parasites from the peripheral blood is often further followed by a disappearance of parasites from the internal organs.

In our own cases, then, we have five autopsies showing recent malarial infection, and 93·8 per cent. of our cases showing undoubted evidence of malarial infection in the peripheral blood.

It has been urged that the occasional presence of parasites in blackwater is accidental and dependent on the fact that the subject of blackwater is living in a highly malarious country.

A considerable number (44) of Europeans living in the tropics were therefore examined by us for evidence of malarial infection, viz., either parasites or pigmented leucocytes or an increase in the mononuclear leucocytes. The result of this examination is given in Table II. It will be seen that most of the communities chosen are those especially liable to malarial fever, and indeed among the Roman Catholic community mosquito nets are rarely used, whilst on both the Lagos and Sierra Leone railways malarial infection is most rife. Yet in the blood of these individuals we find parasites with the greatest rareness, nor are pigmented leucocytes much more frequent. A certain number show a percentage of large mononuclear leucocytes above normal, but most of these do not reach as high a value as in most of the blackwater cases, the blood examination having often been no doubt too late in convalescence to show marked percentages. Those showing parasites or pigmented leucocytes are under 10 per cent., whilst including those with even a poorly-marked mononuclear increase only 20 per cent. show evidence of malarial infection.

It is thus abundantly evident that the malarial infection demonstrable in over 90 per cent. of blackwater cases is not dependent on the accidental occurrence of malaria, but must be a causal connection.

We must accordingly assign to the hæmoglobinuria of the tropics a malarial origin, though recognising that it is by no means a mere malarial attack of extreme severity.

Table I.—To show the occurrence of Malarial Infection in Blackwater.

Cases.	Parasites.	Pigmented leucocytes.	Autopsy.	Large mononuclear leucocytes.	Small mononuclear leucocytes.	Polymorphonuclear leucocytes.	Proof of malarial infection at time.	Parasites present in peripheral blood.	Remarks.
2*	—	pig. leucs.	much pigment.	22·7	14·6	60·7	Yes	No	
3*	numerous parasites	,, ,,	,, ,,	55·9	—	43·0	,,	Yes	22.5.99. Before onset of blackwater.
		,, ,,	—	19·3	—	80·0		No	24.5.99. Shortly after onset.
4*	3 crescents	,, ,,	—	48·8	8·4	41·6	,,	,,	
5*	—	—	—	30·6	7·8	61·6	,,	,,	
6*	—	—	much pigment.	—	—	—	,,	—	Post-mortems only.
7*	—	—	much pigment.	—	—	—	,,	—	Post-mortem only.
8*	—	pig. leucs.	much pigment.	12·0	7·0	80·0	,,	No	
9	—	,, ,,	—	23·6	6·0	68·6	,,	,,	
10	—	,, ,,	—	27·0	19·0	54·0	,,	,,	
11	parasites	,, ,,	—	21·5	16·4	61·0	,,	Yes	12.7.00. Case seen earlier than usual.
		,, ,,	—	11·5	12·0	75·0		No	13.7.00. Blackwater still present.
12	—	—	—	6·4	4·5	89·0	No	,,	Only a single blood examination made.
13	—	pig. leucs.	—	21·0	13·5	65·0	Yes	,,	
14	—	—	—	23·0	23·0	54·0	,,	,,	
15	—	—	—	24·0	13·6	61·5	,,	,,	
16	—	pig. leucs.	—	12·7	10·5	77·0	,,	,,	6.10.00.
				15·5	10·5	74·0		,,	7.10.00.
17	—	—	—	22·7	12·6	64·0	,,	,,	Convalescent, 6 days.

* Note.—See the First Report to the Malaria Committee. Case I is not included on account of the insufficiency of the examination.

Table II.—To show the occurrence of Malarial Infection in Europeans taken at random, more especially from Communities suffering much from Malaria.

			Parasites.	Pigmented leucocytes.	Large mononuclear leucocytes.	Small mononuclear leucocytes.	Polymorphonuclear leucocytes.	Eosinophyl leucocytes.	Proof of existing or very recent malarial infection.	Remarks.
Lagos merchants' clerks.	1		—	—	12·3	17·6	58·6	11·3	No	
	2		—	—	16	20·6	61·6	1·6	?	
	3		—	—	18·6	19·8	61·2	2·4	Yes	
	4		—	—	13	19·5	61·5	6	No	
	5		—	—	10·6	25	62	2·3	,,	
	6		—	—	19·5	19	59·2	2·2	Yes	Slight fever at time.
	7		—	—	15	8	74·6	2·3	No	Fever at time.
Lagos R. Catholic sisters.	8		—	—	13·3	17·6	66·3	2·6	,,	
	9		—	—	11·2	23·2	64·5	1	,,	
	10		—	pig. leuc.	10·6	14·3	67·6	7	Yes	
	11		—	—	10·6	29	57·3	3	No	
	12		Crescent	—	10·5	17·5	71·5	0·5	Yes	
	13		—	—	13·5	23	62·5	0·75	No	
	14		—	—	13	34	51·5	1·5	,,	
	15		—	—	20	15·5	61	3·5	Yes	
	16		—	—	13·2	21·7	61·7	3·2	No	
Lagos R. Catholic fathers.	17		—	—	7	18·5	74	0·5	,,	
	18		—	—	14·5	21	61·5	3	,,	
	19		—	—	13	6·75	60·7	9·5	,,	
	20		—	—	14·5	24·5	56	5	,,	
	21		—	—	10	12·7	73	4·3	,,	

Table II.—*continued*

		Parasites.	Pigmented leucocytes.	Large mononuclear leucocytes.	Small mononuclear leucocytes.	Polymorphonuclear leucocytes.	Eosinophyl leucocytes.	Proof of existing or very recent malarial infection.	Remarks.
Government officials	22			11·3	20·3	67	1·3	No	
	23			13·6	39·3	46	1	,,	
	24			13	20·5	58	3·5	,,	
	25			7·6	15·3	76·3	0·6	,,	
	26			18	26·5	53	2·5	Yes	
	27		pig. leuc.	12	19	66·5	2·5	,,	
	28	Crescents		26·6	19	54	0·5	,,	Fever at time and previously.
	29			12	31	51	6	No	
	30			12·5	22	65·5	—	,,	
	31			12·7	11	74·6	2	,,	
Sierra Leone railway men	32			11·3	17	68·6	3	,,	
	33			20·3	24·3	52·6	2·6	Yes	Temperature 104° day before quinine.
	34			14	18·3	67·3	0·3	No	
	35			13	15	70·6	1·3	,,	
	36			15	20·8	60	4·1	,,	
	37			10·5	14·5	73	1·5	,,	
	38			11	13	72	4	,,	
Lagos Government railway men	39			9·6	11·3	75·3	3·6	,,	
	40			12·6	16·3	50·3	11	,,	
	41			10	21·3	66·6	2	,,	
	42			10·6	11	78·3	—	,,	
	43			13	13·1	65. 4	8·5	,,	
	44			10·2	16·5	69	5·2	,,	

III. *Conclusion.*

1. That blackwater is malarial in origin, yet cannot be considered as an attack of malaria.
2. That quinine is, in the great majority of cases, the proximate cause.
3. That there is not a single fact in evidence of a special parasite being the cause of blackwater. Blackwater more closely resembles paroxysmal hæmoglobinuria, and possibly hæmoglobinuria in horses, than Texas fever.

Protection from malaria, then, would diminish the chances of blackwater fever, and measures directed against malaria would, if successful, tend to diminish the amount of blackwater, which at present is pre-eminently the cause of death among Europeans in tropical Africa.

Malaria is, we believe, a preventible and avoidable disease; consequently the European in the tropics, who thinks it worth while to avoid malaria, will have little fear of being attacked by blackwater fever.

We cannot conclude our report without acknowledging our indebtedness to the medical officers of the colonies we have visited, to Dr. Gray, Zomba; Dr. Kerr-Cross, Blantyre; Dr. Prout, Sierra Leone; Dr. Knight, Accra; Dr. Strachan, Dr. Pickels, and Dr. Best, Lagos. Also to the medical officers on the Sierra Leone and Lagos railways, Dr. Leach, Dr. Rowlands, and Dr. McGahey.

We have especially to thank Dr. McVicar, Blantyre; Dr. Berkeley, Freetown; Dr. Knight, Accra, and Dr. Hopkins, Lagos, for much help and for much trouble undertaken on our account. Also Dr. Scott and Dr. Elmslie, British Central Africa, and Dr. Todd, late of Umtali, for specimens of blackwater cases.

REPORTS, &c., FROM Dr. C. W. DANIELS, EAST AFRICA.

"Some Observations on the Common Anopheles of British Central Africa, the Haunts and Habits of their Larvæ during the Dry Season, 1899." By C. W. Daniels, M.B. Received January 8, 1900.

These observations were made in, and refer only to the Dry Season, April to October. A further series of observations will be required for the Wet Season.

The commonest and most widely distributed Anopheles is a small dark one* with legs of a uniform colour and two light bands on the palpi. It is found at all heights from 4200 feet down to 200 feet above the sea-level. It is also met with all round the Lake Nyassa and down the Shiré River for at least 150 miles. This represents the limit of my observations. In some of these places it is so numerous as to be a pest. In others it is only found with difficulty.

Under experimental conditions it will only lay its eggs on still water. The motion of the surface of the water produced by the wind is quite sufficient to prevent the deposit of eggs.

The eggs are laid on the surface of the water in little clumps. They are separate and lie horizontally on the water. They readily adhere to any solid body with which they are brought in contact. As a consequence of this adhesiveness they are often found adhering to the sides of the vessel containing them, especially if the water has been disturbed by wind or movement. It is probably on account of this property that they are so difficult to find under natural conditions.

The eggs hatch in two or three days. If allowed to dry, or if completely immersed for half an hour, they will not hatch.

The larvæ are very small, and difficult to see for the first two or three weeks. Their habit varies under the different conditions met with, but they usually are easily found in small numbers.

To determine their haunts in the Highlands, I have examined all the waters in Blantyre and the immediate neighbourhood at the end of the dry season, with the following results.

The larvæ are found constantly in the swamps or shallow pools marking the outlets of the springs which form the sources of the

* Since identified by Mr. F. V. Theobald as *Anopheles funestus*.

numerous streams. These pools are usually overgrown with grass. The larvæ are of all ages, from the quite young to the pupal forms. In the streams arising from these springs, larvæ are also constantly found in places where the current is slight, particularly where the water is screened from sun and wind by overhanging banks or grass. When such a stream reaches a level portion and spreads into a pool or swamp, the larvæ are often abundant, but not if the water is stagnant or markedly peaty.

The larvæ are of different ages, but I have not observed very young forms in the streams. This suggests that the larvæ in these situations have been carried down from the springs; but as they are found day after day in the same places and sometimes as pupæ, these streams, if they are not actually the breeding grounds, at least distribute the mosquitoes and allow the further development to take place.

Several of these streams join to form a small rivulet, the Mudi, which is in places several yards wide. This I have followed for some three miles, and all along at points have found these larvæ.

The larvæ are also found in irrigation trenches used for gardening purposes, under similar conditions to those found in streams.

In none of these springs, streams, or trenches did I find any fish, so these must be rare. The natives say there are some, but that they are not abundant in the upper reaches.

These breeding grounds abound in the Highlands, even after prolonged dry weather. In an area of about two square miles I found no fewer than eleven of these springs, and I know of four others now dry which were active early in the dry season, and from the lie of the ground it is certain that there were many more in the first months of the dry weather.

On leaving the Highlands true rivers are found. These run into the Shiré, which rises from Lake Nyassa. The Shiré and these rivers swarm with small and large fish.

The Shiré, as traced from the lake, shows the conditions under which larvæ are found in waters swarming with fish. The river is the main if not the only breeding ground of the mosquitoes, as they are found at no great distance from the banks, and their prevalence varies with the favourable nature or otherwise of the conditions in the river for the existence of the larvæ.

The Shiré River on leaving the lake runs through low, sandy, alluvial land. The banks are usually low, swampy, and covered with rank grass and reeds. Any holes, such as hippopotamus tracks, are filled with peaty water. In these holes I have never found the larvæ, and the water, if added to that in which larvæ are growing, will speedily kill them.

From the edge of the banks grows a short grass which extends right out into the stream, sometimes for 20 yards or more. This grass is

supported by a close meshwork of floating but submerged roots. Masses of this grass may become detached from the bank and form floating islands. Above the false bottom formed by the close meshwork of floating roots is shallow water, into which fish will not have ready access; in this water the Anopheles larvæ, of all ages, are found. They are not found in great numbers, but are found constantly, and are more numerous near the bank. Where this grass abounds the mosquitoes are numerous, even after months of dry weather, when the river is at its lowest, and all other water is gone.

Lower down, the Upper Shiré expands into a shallow lake, Lake Pamalombi, covered with tall reeds in great part. The floating grass is not abundant. In the wet season mosquitoes are very abundant, but are not very plentiful at the end of the dry season.

Below this lake there is little grass with floating roots; its place seems to be taken by a coarser grass rooted in the bottom, but also throwing out plenty of aqueous roots, so that a meshwork, though not very close, is formed. I found larvæ amongst this in places where it was thick. In the later part of the dry season the mosquitoes here are far less numerous than in the early part, when there are extensive swamps.

So far this Upper Shiré is navigable from the lake. It is about seventy miles long. The next portion, the Middle Shiré, is a series of rapids seventy miles long with a total fall of some 1200 feet. The current varies greatly. In some places the stream is slack enough to allow of a ferry, and in one of these places there was abundance of this fixed grass. Here the Anopheles were found. The same grass was seen in patches all along the river. In one part the river flows through deep rocky gorges with great rapidity; we camped here for the night, but found no mosquitoes.

On the west bank, at the time I was there, there were only two rivers running into the Shiré; in one of them there was much fixed grass, and on its banks there were plenty of Anopheles. The other had a rocky bed, and I am informed that there were no mosquitoes there.

Below these rapids is the Lower Shiré, navigable from the sea. The fixed grass was very abundant here, but the Anopheles were not very abundant, though both the larvæ and adults were found without difficulty. The climate is very different on the Lower river and much hotter. Culices of several species, including a large yellow one which carries the *Filaria nocturna*, abound.

The only other important water is Lake Nyassa, 1540 feet above the sea and 350 miles long. No mosquitoes are found in the open. The banks at the places I visited were fringed with reeds. There was no floating grass and very little grass growing into the lake. Mosquitoes are rare in many places on the lake shore.

In the lake itself I found Anopheles in one place only.* This was in a sheltered bay where the reeds extended for a long distance out. The larvæ were not found among the reeds, but just at the edge of the lake, where grass was growing and a kind of small water-lily.

At this time the streams running into the lake were in many cases dry or reduced to a series of stagnant water holes, in which no larvæ of Anopheles were found. In other places there was a series of water holes with a small stream connecting them ; in some of these the larvæ were found. Replacing the end of the stream in some places was a small pool at the lake level, but separated from it by a sandy bar. In these pools the larvæ were constant.

The different situations in which the larvæ are found under these diverse conditions have points in common. In all, the water is fresh, and kept so. It is more or less permanent. Fish are scarce, or the larvæ are protected from them.

I have at times found the larvæ in small pools without any connection with other water, and the larvæ were sometimes over two weeks old. In some such puddles, which I was able to watch, the larvæ soon died or the puddle dried up. In the last case the larvæ were not restored by adding water. As the shortest period I have observed for the larvæ to reach maturity has been thirty-two days, the chances of such larvæ reaching maturity in the dry season must be very small. Even pools large enough to contain water all through the dry season after a few months become stagnant, and larvæ are not found in them.

Observations made on larvæ under artificial conditions explain in the main the reasons for the natural distribution. The constant motion of the lake would be unfavourable for the laying of eggs. The eggs when laid would be carried by the waves and attached either so high that they would be dried, or so low that they would be submerged, and therefore not hatched.

The length of time required for the growth of the larvæ with their susceptibility to stagnation explains the need of some permanent fresh-water supply. In captivity fresh water has to be added almost daily, or they will often die.

There is no difficulty in understanding how the larvæ are able to exist in running water. If larvæ be placed in an open vessel when there is a strong wind blowing, the water is put into rapid rotation ; but the larvæ, without any apparent motion, are able to maintain their position, adhering by their tails to the side of the vessel. If attached to a floating object it will rotate with the water, and the larvæ with it, without any signs of inconvenience. They are also able to move against a strong current for short distances.

* Subsequently, in 1900, I found Anopheles larvæ in many similar places at the Lake edge.

The conditions inimical to their existence are stagnation, putrefaction, or peatiness of the water. Their most important natural enemies are small fish. In addition, the larvæ, either of the same or a different species, will at times devour a younger one. If Cyclops are very numerous they will destroy the very young, but not the older larvæ.

There is one condition under which I have uniformly failed to find these larvæ, though those of Culices may be found, and that is in wells, unless the surface of the water is flush with the ground. The native wells are mere holes dug in the ground at or below a spring. In the dry weather the water-level is below the surface of the ground, and only Culices, if any larvæ at all, are found. The European wells are brick and are often covered. It is exceptional to find any larvæ at all in these, and those are not Anopheles. To kill the larvæ it is not necessary to dry them. If the superjacent water be poured off, they will not live more than a few hours in the liquid mud. Advantage might be taken of this to kill the larvæ in irrigation trenches, as diverting the water for a few hours two or three times a month would probably kill off the larvæ in it.

The breeding grounds in the wet season will have to be a specia study, but with our present knowledge it is probable that in the Highlands they will be confined to the springs, but those will be both more extensive and more numerous.

In the river the floating grass will be little affected, but extensive areas near the river will be flooded, and there the larvæ will be able to live during, and for some time after, the wet season, till the water becomes peaty or stagnant.

The adult mosquito bites mainly at night, but occasionally in the day. Unlike many of the Culices it does not leave the house in the day, but will be found at dawn near the bed. When disturbed it flies upwards, so that by the time a room is swept out, or a free current of air established, it will be found high up on the wall only.

Prophylaxis.—In a well-watered country any complete extinction of the species would appear to be impracticable.

In any given area they might be exterminated or much reduced. This will be costly in such sites as Blantyre, with numerous springs and rivulets.

Probably the best means would be the erection of wells with a clear pipe or brick overflow below the surface of the ground wherever there is a spring. The streams themselves should have their banks kept clear of brush and long grass, and places where the stream spreads out into a marsh have a graded drain through them. In the rivers the floating grass should be detached for a considerable distance above and below any settlement early in the dry season. If the long grass and reeds were cut down and the banks kept clean, the period during which the mosquitoes are prevalent would be much reduced.

Some of these measures are required on other grounds. In the bush surrounding the sources of the rivers and streams is much filth, as it is used by the natives as a latrine.

More wells are required, as the water supply is inadequate unless much fouled river water is used.

The houses should be better ventilated, and top-ventilation introduced to give the mosquitoes fewer resting places in the houses. The narrow beds and mosquito curtains allow the mosquitoes to bite any part of the body which comes in contact with the net. In the morning numerous mosquitoes gorged with fresh blood are usually found on the outside of the net. The small mosquito-proof room with the bed inside is much safer.

Larvæ of other Anopheles are much rarer, but I have found them in the springs, and the streams running from them, so that they seem to have similar habitats.

"Distribution and Breeding Grounds of Anopheles in British Central Africa." By C. W. Daniels, M.B. Received June 7, 1900.

In continuation of my report on the breeding grounds of Anopheles for the Dry Season, April–October, 1899, I have the honour to report as follows for the Wet Season, October 1899–March, 1900 :—

The observations for this second period are in the main confirmatory, and in parts explanatory, of the observations in the previous dry season.

2. The observations were made in the Shiré Highlands at Blantyre, my headquarters during some portion of each month, and Zomba, in January, February, and March.

On the Upper Shiré (lake level) November, December, and March.

On the Lower river in February.

3. The increase in the number of mosquitoes has not been very marked at most places, except at Zomba. With the first onset of the rains there was an immediate decided increase in the number of mosquitoes infesting the houses. This, I think, was probably due to the mosquitoes seeking a more secure shelter than that afforded by grass, &c. This increase was not maintained; on the contrary, at Matope (Upper river) in November and December, fewer mosquitoes were found in the house than in May or September, when I had been there before.

The Breeding Grounds.

4. The wet season commenced unusually early (in October), with days of heavy rain alternating with periods of rainless weather. This weather continued till near the end of November. During December,

January, and the early part of February the rains were more continuous, and the periods of rainless weather shorter.

Since then the periods of fine weather have again been longer. The attached table shows the amount and distribution of the rains during the period under review. Perhaps the clearest way of indicating the effect of this season is to take as an illustration a single small drainage area. The one nearest is selected for description, as that is the one most constantly under observation, but the results have been confirmed by frequent periodical examination of other known breeding places in the immediate neighbourhood, and by numerous isolated examinations over 100 miles of road in the Shiré Highlands. The place is some distance from the mountains, and in gently undulating country. Down the hollow, the water during rains pours into the Mudi (the small river separating Mandala and the hospital from Blantyre and the Scotch mission). The position of this stream is marked by the belt of trees in the photograph*. The height of the ridges surrounding this hollow marks the watershed between this and another small water system. In the views taken, this adjoining water system runs nearly at right angles, though the water from it is also poured into the Mudi. About half way down the gully is a spring permanent all the year round, and round about it a swamp. This swamp, as is usual, is overgrown with tall blue grass, which here and elsewhere indicates permanently wet soil. It is further indicated in the photo by the natives who are standing just above it. From this spring a small stream runs to the Mudi, spreading out in places into shallow swamps, and in others overgrown and blocked with grass.

About the source of this spring and in places in its course where it spreads into shallow swamps, or in dry weather is running very slowly along the grassy edges, Anopheles larvæ were found constantly, both at the end of the dry season and all through the wet.

Above this permanent spring is a natural cutting dry from May to October, except during and immediately after showers.

In the early part of the wet season after each period of rain it soon dried up, in each spell of dry weather leaving a few small pools in which, up to late in November, no Anopheles larvæ were found. Towards the middle of December, even in dry days, water was to be found oozing from the sides of the cutting in places, and consequently the channel never became dry.

In many parts of the course of this cutting grass had grown, and in level portions shallow pools were formed, and from the end of December Anopheles larvæ were found constantly in such places.

In this valley were several deep pits left in brick making, and one of them was deep enough to contain water permanently throughout this

* Not reproduced.

season. These pits have all red clay walls, and usually little vegetation ; they are common throughout the Protectorate, as most of the houses are built of brick, but in none of them have I found Anopheles larvæ.

Towards the head of the valley there is a swampy area much trodden by cattle ; in their tracks water collects, and will withstand several days dry weather, but no Anopheles larvæ were found in them. On the left-hand side of the valley, looking down it, is the public road. On each side of this is a cutting to carry off the water in rainy weather. With constant rains they are scoured out, and after two or three days dry weather they are dry. No Anopheles larvæ were found in them.

On the right-hand side of the road there is a small extent of flat land ; on this ephemeral puddles only form, and in them no larvæ were found. There is also a cattle pond formed in red clay like the brickfield ponds ; in this Culices in abundance, but no Anopheles, were present.

This valley fairly represents the usual conditions in the Shiré Highlands in the neighbourhood of Blantyre ; and in the area of about two square miles, including Blantyre township, the Blantyre mission, Mandala, and the Blantyre hospital, there are some fourteen similar small valleys. In some there are two springs, in others the slope from the springs is steeper, and larvæ are only found near the springs, and in others the springs dry up before the end of the dry season.

The Anopheles larvæ found were not all of one species. In the valley I have taken as an example, larvæ of all the five Anopheles found in these Highlands were found at one time or another. In no other valley have I found the same number, but two or three species were commonly found together, and sometimes four. As the associated species differed at different times and in different places, I consider that all the Highland Anopheles have similar breeding places, and that the five were found in this valley was probably due to the more frequent examinations made.

The commonest larvæ found were that of the so-called "small black" Anopheles.

In my report on the dry season I pointed out that the Mudi itself, though a running stream, contained these larvæ.

With the onset of the rains this stream was converted into a muddy torrent. At first, with each period of dry weather, the river fell rapidly and became clear, and the Anopheles were again found in the same or similar sheltered positions to those of the dry season. This observation was repeated in several places, both on the Mudi and in other streams, in several of the dry periods in the first six weeks of the rains, and leads me to believe that the larvæ are washed down from the springs to such situations, rather than that they have been actually bred there.

The importance of this difference will be better considered in connection with irrigation trenches.

By the middle of December the level of the stream was permanently decidedly raised, and the force of the current uniformly great. In spells of dry weather the water became clear, but the level never low. From that time onward larvæ were never found in the stream, nor in any of the other permanent clear streams I visited.

In Zomba the conditions are different, though the general principles are the same. Zomba is situated on the south-western slope of a mountainous plateau (Zomba mountain), some 6000 feet high: it is about the same level as Blantyre (3200 feet high), and a few hundred feet above the table land (Shiré Highland) to the south. There are numerous springs, but instead of being in definite valleys they are rather extensive swampy areas, probably dependent on subjacent rocky fissures. In these areas Anopheles larvæ were found.

The natural streams running from them were free from larvæ, and the slope is so steep that it is improbable that larvæ could remain in them.

For drainage and irrigation purposes an extensive network of trenches had been cut. Many of these are nearly horizontal, and others have been neglected and allowed to become blocked, overgrown with grass, or leaky, so as to form small swampy areas.

In others, again, the area to be irrigated is too extensive for the water supplied, so that in portions the water is practically still even in heavy rains. In all these classes of situations, Anopheles larvæ were found.

There was a marked difference between irrigation trenches in which the water was derived from a clear running stream, and in those in which the water was the drainage of an Anopheles-bearing swamp. In the former, Anopheles larvæ were only found where the conditions described were present in a gross form; in the latter, when there was sufficient pause in the rains for the water to become clear, they were found in any place where the current was slack.

This affords a further and more conclusive reason for considering the larvæ in trenches to be in part carried down from the true breeding grounds. They are washed down by the rains and accumulate in suitable places. In trenches—as roadside ones, where the water soon dries up—Anopheles are sometimes found, in and only in the vicinity of an Anopheles swamp.

On the Zomba plateau itself are a few houses, used as a sanatorium, at a level a little over 5000 feet. This portion of the plateau is gently undulating, and in one place very similar to the places round Blantyre I found Anopheles larvæ. They were found with difficulty and in very small numbers, though the local conditions were favourable. It is therefore probable that this height, is, in this latitude, near the limit suitable for the breeding of these mosquitoes.

In the broader flat valleys in the Highlands there are in the wet season extensive swamps; in these, Anopheles larvæ are rarely met with.

I had anticipated finding Anopheles larvæ in open puddles during the wet season. In only one instance did I find them, and that was in a shallow excavation not penetrating through the black soil, and near a stream, but not supplied by it or by any other stream. In this, numerous Anopheles larvæ and some Anopheles pupæ were found, but this was after a month with hardly a rainless day, and in low land on the low banks of a stream. On the Upper and Lower rivers (Shiré) Anopheles larvæ were found, as during the dry season (among the grass growing in shallow water, and in that on the floating grass prevalent in the Upper Shiré above Lake Pamalombi).

The river was considerably higher and the current stronger, in one place (Chikwawa) said to be three miles an hour.

In the marshy ground where in the dry season the water was stagnant or peaty, the abundant rains had in places reduced this condition, but in no instance did I succeed in finding Anopheles larvæ. Frequent examinations were made in many different places with negative results, but considering the extent of these swampy areas during the wet season, I cannot consider my negative results as conclusive. In some parts of them, at least, the conditions must be favourable for their development.

On the Upper Shiré only one Anopheles (the "small black") has been found by me.

On the Lower river the "small black" is also found, and in addition three others different from those in the Highlands, and in the river there three kinds of larvæ were found—those of the "small black" and two other kinds—which, however, I failed to rear. It is therefore probable that in the Lower river the different Anopheles have similar breeding grounds as is the case in the Highlands. The lake I was unable to visit.

I have paid particular attention to all kinds of puddles during this wet season. The instance given above is the only one I have met of larvæ being found.

In some instances, in small grass-grown hollows which only overflow with heavy rains, but into which water runs with slight ones, larvæ were found during the time when there were few successions of dry days. Such places are rare.

I subjoin a table showing the places in which larvæ have been found in the Protectorate in the year under review.

To a large extent, not only each country and district but even locality differs in details. The slope of the ground, its nature and permeability, will largely determine where water, suitable for the breeding of these mosquitoes, will be found, and whilst in British

Table showing Rainfall and Distribution of Rains during the Year in Two Places in Districts Nos. 2 and 3. The figures for Fort Johnston are for the previous Year; those for 1899—1900 were not obtainable.

Zomba. Shiré Highlands.

Month.	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.
Rainfall for month	9·75	2·7	0·51	0·07	0·1	0·12	2·23	13·40	7·79	15·94	2·19	5·76
Number of days on which rain fell	18	12	6	3	1	1	4	19	21	25	11	12
Longest period without rain	4 days	7 days	19 days	28 days	30 days	29 days	12 days	5 days	4 days	Under 2 days	6 days	15 days

Fort Johnston, Upper Shiré (Lake Level).

Month.	April.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.
Rainfall for month	0·38	*p*	0·2	0	0·12	0·05	0·38	1·73	8·66	7·54	8·68	6·89
Number of days on which rain fell	3	1	2	0	1	1	1	9	14	22	14	17
Longest period without rain	10 days	27 days	28 days	31 days	20 days	29 days	30 days	8 days	4 days	4 days	3 days	4 days

There were 79 days (consecutive) without a shower in these three months.

Description of Places.	Dry season, July to October.		Onset of rains, October to December.			Wet season, continuous.			Drying-up season, April to June.		
			Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April.	May.	June.
The Lake Shore—											
A. Clear, or only fringed with reeds.	0	0	0					0		0	0
B. Behind sand bars separated from lake.	+	+									+
C. Among thick vegetation		+									
Shiré River—											
A. Open water	0	0	0	0	0		0	0	0		0
B. When sheltered by grass...	+	+	+	+	+		+	+	+		+
Swamps in Plains	0	0	0	0	0	+	+	0	0		0
Large Streams (Mudi, &c.)	+	+	+	+	0	0	0	0	0		
Slow Small Streams—											
With slow current, or blocked in places.	+	+	+	+	+	+	+	+	+		
Irrigation Trenches	+	+	+	+	+	+	+	+	+		
Springs—											
Permanent all the year round..	+	+	+	+	+	+	+	+	+	+	+
Permanent in the wet season and early dry season.					+	+	+	+	+	+	
Puddles—											
Permanent in wet season.....			0	0	0	+	+	0	+ on the Zambesi		
Native Wells	Very rare, and only when the water level was nearly that of surrounding ground.										
European Wells.....	None found at any time.										

0 indicate that larvæ were not found. + indicates that larvæ were found. *No entry* that no sufficient examination was made; in some cases because none was possible; in others, as in April and May, because I did not then know in what places to look.

Central Africa a porous, rocky, or sandy soil, and low-level subsoil water, prevents puddles being an important breeding ground except under exceptional circumstances; under other local conditions, even with similar meteorological factors, they may be the leading one.

The obvious presence of Algæ is no necessity; on the contrary, if abundant, Anopheles larvæ are rarely found.

The kind of grass growing from the shallow water varies; when very tall, as the blue grass mentioned as forming a guide to the spring, they are only found at its edges, and more frequently in places amongst it where there is open water. In the floating grass in the Upper river they are more readily found some distance from the edge. This grass is only about one foot high out of the water. In the fixed grass below Lake Pamalombi, and in the Lower Shiré, they are rare, except for about a yard from its edge. This grass is several feet high. The differences are most probably dependent on degrees of light and shade, either directly, as affecting the larvæ, or as affecting the growth of suitable foods.

Prophylaxis I deal with separately.

Breeding Grounds of Anopheles in British Central Africa.

(Supplementary Report.)

(Received January, 1900.)

Since I forwarded my Report on this subject, I have received copies of the 'British Medical Journal,' giving the results of similar investigations at Sierra Leone.

It is clear at the outset that we are dealing with different mosquitoes.

It may appear from my Report that little attention has been directed to "puddles." This was not the case. I was familiar with Ross's observations in India, and the first evidence I had of the existence of Anopheles in Africa was the presence of larvæ in a puddle on the way up the Zambesi. I failed to rear these larvæ.

In British Central Africa at first I mainly directed my attention to puddles, and it was only when I failed to find them there that I systematically looked elsewhere.

In the Upper Shiré district the soil is very sandy, and it is practically rainless for months; so puddles do not exist, unless the marshy tracts below or at the level of the river can be so called. In these, at any rate when the dry season is advanced, as I have already pointed out, the water is too peaty or stagnant for the larvæ to exist.

The suggestion has been made that the mosquito eggs may remain dormant for considerable periods. This is not the case here, as unless the eggs hatch within a few days they do not hatch at all.

No definite relationship between Anopheles breeding grounds and human habitations obtains here. The country is thickly populated, and native villages are always near permanent water, and consequently usually near Anopheles breeding grounds; but breeding grounds are also found at considerable distances from any dwelling.

Kerosene, as a laboratory experiment, readily kills the larvæ, but its application to the actual breeding grounds here is impracticable, as the water supply of the people would be affected.

The alterations produced by the wet season, so far, are as anticipated. The swamps surrounding springs are larger, and so the breeding grounds more extensive. They are also more numerous, as springs previously dry are now running. In some of these the larvæ were found early in the dry season, but not at the end of it. They are now again found, but only young forms.

The streams are fuller, and running stronger, and larvæ are now no longer found in them.

Development of "Crescents" in the "Small Dark" Anopheles prevalent in British Central Africa.

By C. W. Daniels, M.B. Received March 5, 1900.

The following observations were made on mosquitoes fed on an adult male European who had had "fever" off and on for a month. The first blood examination was made on November 23, and crescents only were then found. At that time and on the following morning he had fever, which left him in the evening. Crescents continued to be present in fair numbers, usually five or six in a fresh blood slide, and on November 26 I took him to Matope, on the Upper Shiré River, as there the Anopheles* I wished to experiment with are usually plentiful.

He remained at Matope for eight days. The mosquitoes (Anopheles) were far less abundant than at any of my previous visits, and a considerable number were required for control experiments, so I was only able to feed sixty-eight on the patient.

Of these sixty-eight, five died at various periods after feeding, but were too dry and brittle for dissection. Six died within thirty-six hours of feeding; these did not have any zygotes. The remaining fifty-seven died from two to nineteen days after feeding on the patient, and were examined—twenty-seven, or 47·5 per cent., had zygotes.

* Identified by Mr. F. V. Theobald as *Anopheles funestus*.

The temperature varied from 70°—84° F.

This percentage is in excess of the true proportion of infections resulting from a single feeding, as most of the mosquitoes were fed on the patient more than once.

Nineteen had been fed once only—five, or 26 per cent., had zygotes.

Thirteen had been fed twice—six, or 46 per cent., had zygotes.

Sixteen had been fed three times—ten, or 62 per cent., had zygotes.

Nine had been fed four times—six, or 66·6 per cent., had zygotes.

In all, the fifty-seven mosquitoes had fed 129 times, and in many of the mosquitoes the zygotes were of different sizes and stages of development, corresponding to different feedings.

In the five fed once, the zygotes were all of the same age.

In the six fed twice, the zygotes were of one age in three, and of two ages in three.

In the ten fed three times, the zygotes were of one age in five, of two ages in two, and of three ages in three.

Of the six fed four times, they were of one age in two, of two ages in one, of three ages in two, and of four ages in one only.

So that 129 feedings resulted in forty-six infections, or 35·5 per cent. This is quite as large a proportion as I think could be expected from a moderately good "crescent case," considering the very small capacity of this mosquito's stomach.

The zygotes in general appearance and course of development resemble those of Proteosoma.

The earliest forms, those found towards the end of the second day after feeding, were 7 to 9 μ in diameter. They were oval, had no defined capsule, and only stained faintly with basic stains. The pigment, relatively abundant in some, retained a close resemblance to that of the crescent. In some, even at this age, there was evidence of division of the protoplasm.

The zygotes steadily increase in size, and by the fourth day measure 20—25 μ. A capsule was now distinct, basic stains were taken readily, and the pigment had no characteristic arrangement. They obviously project from the outer wall of the stomach.

Beyond increase in size there was little change on the sixth day, by which time they measure 30—35 μ. Some were slightly granular.

On the eighth day the granular appearance was marked and general. Pigment had diminished, and they measured 40 μ and more.

The capsule can readily be ruptured, but the contents when expressed were only a granular mass.

On the tenth and twelfth days the cysts have reached their maximum size, 50—55 μ, as measured uncompressed and without a cover-glass.

When the capsule was ruptured, the contents of the cyst were poured out into the surrounding fluid. They partly consisted of free filaments, zygotoblasts (Ross's germinal threads), but mainly of clear

spherical bodies with irregularly radiating masses of filaments attached by one extremity.

The arrangement of filaments attached to central body seemed to me conjectural in Proteosoma, but was clear in these cases. Zygotes were traced up to this stage in eight mosquitoes.

Only two were traced further. Both of these had been fed more than once, so the ages are uncertain, 12—16 days in one fed three times, and 14—19 days in the other, also fed three times. In both, a ruptured and other unruptured cysts were found in the stomach, zygotoblasts were present in the body fluids, and in a few cells only in the salivary glands.

No bodies resembling the "brown spores" were present, but the observations were too few for this negative evidence to be of value.

The mosquitoes used were not reared from eggs or larvæ, and may have fed on other animals before feeding on the patient.

Though I should have much preferred to have used such mosquitoes, I do not consider that the results are at all invalidated, for the following reasons :—

Quite young forms, 7—9 μ in diameter, were found in several many days in captivity, in one case ten days, but two days after it had last fed on the patient, and in others after eight, six, and four days' captivity. Mixed infections were found only after repeated feedings on the patient. In those fed otherwise (on self) the infections were single.

The frequency of infection varied with the frequency of feeding on the patient.

Control experiments all gave negative results. These were as follows :—Twenty-two mosquitoes before the arrival of the patient. During his stay, thirty-eight from the room on his right occupied by myself ; and twenty-four from the room on his left.

Thirty-nine others were fed on myself only, and examined four to eight days after the first feeding.

When the patient left, the mosquitoes were smoked out of the room, but on the second day sixteen were found in it and examined.

This gives a total of 139 mosquitoes, and zygotes were found in none, as against fifty-seven with twenty-seven positive results when fed on the patient.

To this I may add a large series of examinations of these mosquitoes in the past few months with negative results in all but one instance. In that already recorded a zygote was found in one out of four mosquitoes fed on a poorer crescent case than this.

The other known pigmented parasites in the district are Proteosoma, which is rare, and can be excluded, as its life-history is well known, and zygotes of such early development are not found so long after

feeding. Halteridium is common, but it is not carried by this mosquito —at least my experiments with it have failed.

Of unknown parasites we can, I think, safely infer that in any in which the later stages are so similar to those of known parasites, the early ones will also be similar.

Other mosquitoes:—

Of a large grey Culex, found in the Highlands and Upper Shiré, fifteen were fed on the patient, in some cases several times. No zygotes were found. The blood capacity of this mosquito is considerable, so these negative results are of value.

Three specimens of a brilliantly speckled, black and white Culex also yielded negative results, and early in the year I fed several of the large yellow, filaria-carrying Culex of the Lower Shiré, and two species of Anopheles, on a richer crescent case than this, in all with negative results, but the numbers of mosquitoes used were too small for the results to be conclusive.

"Notes on 'Blackwater Fever' in British Central Africa." By C. W. Daniels, M.B.

(Received November, 1900.)

The following notes refer only to cases in the above district. I have included in them cases observed by others as well as those seen myself, and am particularly indebted for much information to the medical officers, both of the Administration and the various missions, as well as for much assistance from others.

Occurrence.—The disease affects Europeans and Indians. During the year, June 1899 to June 1900, there were 33 cases, 31 in persons of European descent and 2 Indians.

The *European* population in 1898 was given as 338. It is probably still under 400, so that some 8 per cent. of the European population had this disease in the year.

The *Indian* population, Sikhs and others, is about 200, so that the proportion attacked was 1 per cent. This is probably above the true figures, as with a nearly stationary Indian population there have only been 6 cases in the past 5 years amongst them.

*Natives** (Negroes).—Opinions are divided as to the occurrence of the disease in this class. None of the medical men have seen a case. None of the adults in the armed forces (including carriers: these average upwards of 1000); none of the adults attached to missions, nor of the children attending mission schools, have been attacked. These would average some thousands.

It has not been seen amongst the numerous infants and children

* *Vide* Note 1 (p. 62).

brought to the missions for medical advice. Inquiries were made from 214 native mothers who have lost amongst them 313 children. They deny the existence of such a disease amongst the children, or of any of the deaths being due to it.

It can therefore, I consider, be concluded that this disease is at least of great rarity amongst the native negroes, and is much commoner in Europeans than in Indians.

Sex.—Both males and females are liable to the disease. Of 136 persons known to have had blackwater fever, 9 were females, or 1 in 15. At present the men (Europeans) seem, from returns received, only to be eight times as numerous as the women.

From this it might appear that the men are the more susceptible, but the figures are not conclusive, as the cases are collected from records of many years, and the proportion of females has increased of late. The greater number of women also are resident in the Highlands, and travel less than the men.

There is nothing to show that, under similar conditions, women are less susceptible to the disease than men.

Age.—The number of European children resident is small. Of those born the majority either die, are invalided, or early removed for prudential reasons. The only child attacked was a half-caste (European and native), aged about 5. The ages of the persons attacked vary from 19 to 38, the common age-limits of the residents.

Length of Residence.—This has a decided influence. Few cases occur during the first 6 months' residence. During the second half-year the number rapidly increases. They are most numerous during the second and third year, and become rare after 5 years' residence.

I can find no recorded first attack in any person resident more than 10 years. The number resident over that period is small.

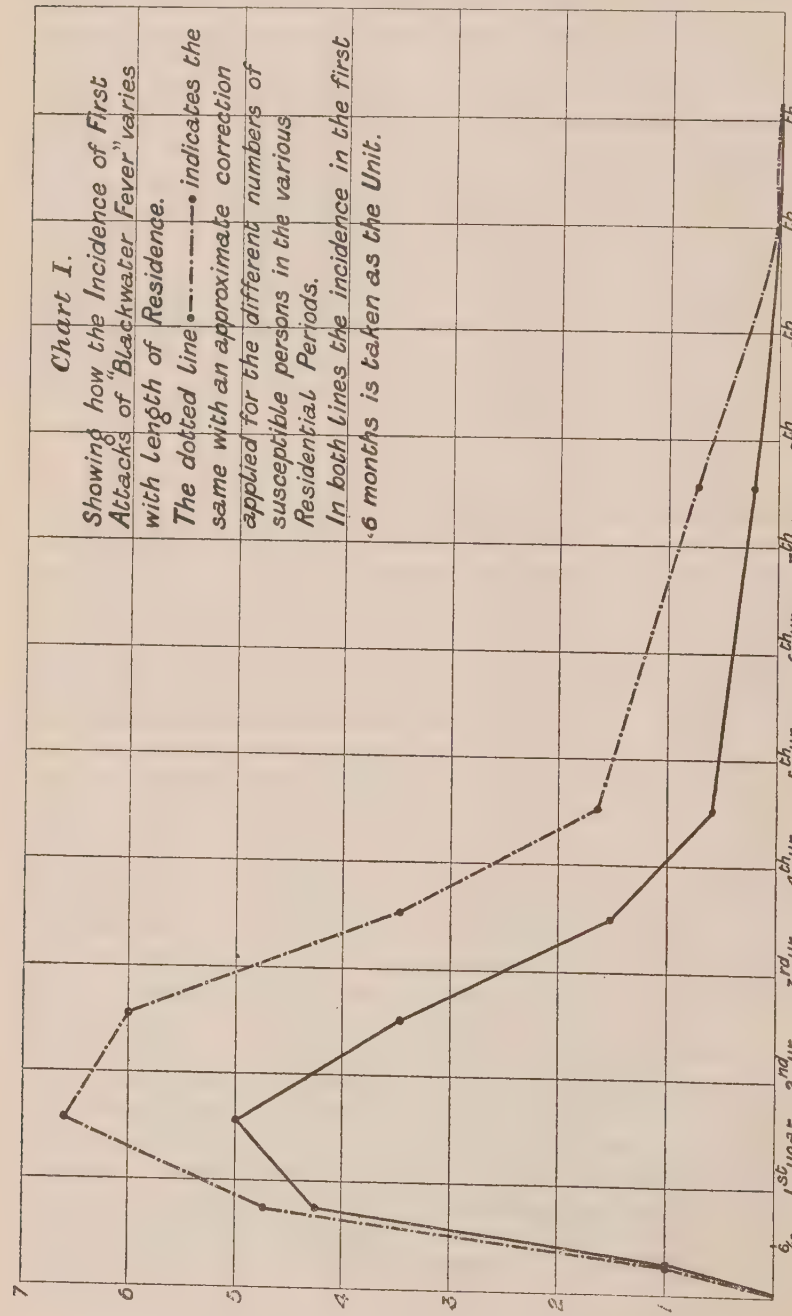
The attached chart (No. 1) shows the variation for the period of residence. The incidence in the first half-year is taken as 1.

Out of 114 first attacks, where the information on this point is sufficiently definite, 4 were in the first 6 months, 17 in the second half-year, whilst for the 2nd, 3rd, 4th, and 5th years the numbers were 40, 27, 12, and 5 respectively. There were 9 cases from the 6th to the 10th year, and none after that length of residence.

A correction is required, as the number of persons in any residential period steadily diminishes. Many leave after the first term of service and do not return. This term of service varies from 2 to 5 years. Others are invalided, and some die or leave for other reasons earlier. Taking the figures obtained from the returns received from 242 residents as representing the numbers of persons of the different residential periods, we have an approximation to the true correction.

The effect of this correction is indicated by the red line in the Chart (1). It does not materially affect the character of the curve.

According to both the corrected and uncorrected figures the liability to the disease is less after 5 years' residence than in the first 6 months.



Districts.—The greater number of the recorded cases have occurred in the Highlands at or about 3000 feet above the sea-level. For this there are two reasons. *First.* The number of residents in these Highlands is much greater than in the other districts. The correction for this alone reverses the figures. *Secondly.* Many of these cases were residents of other districts, visiting the Highlands for a change on account of ill-health, or for other reasons. Others were passing through the Highlands on their way home, sometimes when invalided home. Even of the Highland residents some of the attacks followed a short time after a visit to the lower lands.

On the other hand a few of the cases were in persons from the Highlands, attacked during a visit to other places. A true correction that would attribute each case to the district in which the disease was acquired is impossible. We know on the one hand that it may occur less than three months after arrival in Africa and also that attacks, and even first attacks, may develop months after leaving the country. The latent period may be long or short, and is variable.

Taking an arbitrary period of a fortnight as representing a not improbable latent period in a fair proportion of the cases, we should then find that the place of residence a fortnight or more previous to the attack would give a very different district-distribution of "blackwater fever" to that given by considering the place of onset.

In 97 cases (all 1st attacks) I have sufficient information on these points. The attack of "blackwater fever" commenced in 45 of these cases in the Highlands, in 40 at the Lake Level (Lake Nyassa and Upper Shiré River), and in 12 on the Lower Shiré River.

The susceptible (European) population is, in round numbers, 250 in the Highlands, 70 at the Lake Level, and 50 on the Lower Shiré River. I believe that this substantially represents the relative population of these districts for some years past.

It follows that if allowance be made for the number of susceptible persons in each district a very different district-incidence will be obtained.

Thus on the Lower Shiré, for each 10 persons residing there, 2·4 cases are on record; at the "Lake Level" for each 10 there have been 5·7; and in the Highlands for each 10, only 1·8 cases are recorded.

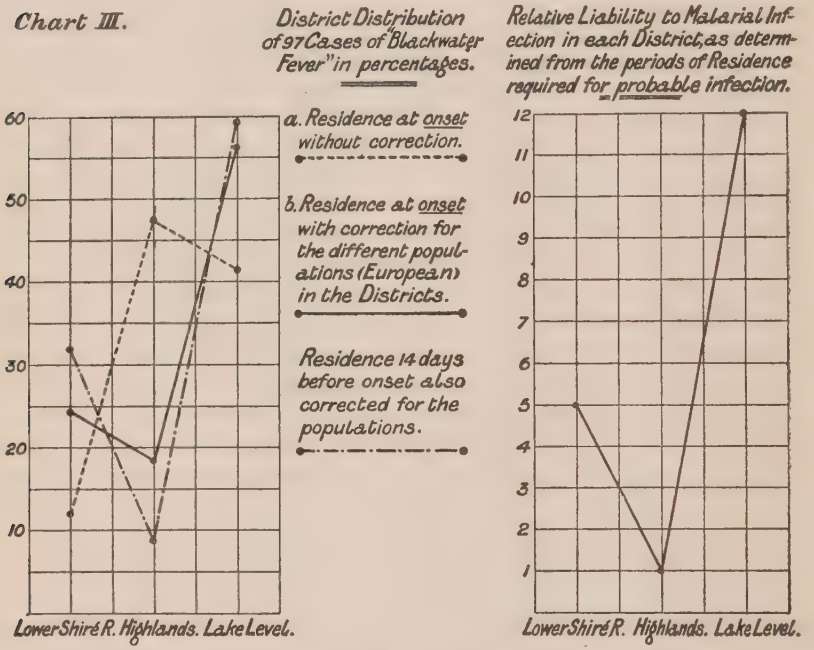
If we take the incidence in the Highlands as 1, that at the "Lake Level" will be 3·16, and on the Lower Shiré 1·33.

Some of these cases occurred immediately after arrival in a district, and should probably be credited to the district they had left. If we take the place of residence 14 days before the onset of blackwater fever instead of the place where the attack occurred, we find that of these 97 cases, 26 were resident in the Highlands, 51 at the Lake Level, and 20 on the Lower Shiré River 14 days before the attack commenced.

Corrected as before for the proportional numbers of susceptible

persons in each district, we find that for each population of 10 there were 1·04 cases recorded in persons from the Highlands, 7·28 from places at the Lake Level, and 4·9 from the Lower Shire River.

Again, taking the Highlands as 1, the proportion from the Lake Level is 7, and from the Lower Shire is 3·8. Chart III indicates these relations.



Whether these corrections, particularly the second, are too great or too small I am not in a position to state. A correction is essential and I introduce these figures, admittedly inaccurate, because conclusions as to the prevalence of the disease in different districts have been drawn on the mere totals without considering the obvious fallacies. Such conclusions are misleading and not warranted by the facts.

The correction is right in principle, and in the right direction. I believe that it does not go far enough. Such cases as one in which a person free from fever left one Highland district, spent some three weeks at the Lake Level, where he had "fever," and then after three months in another Highland district, got "blackwater fever," should be assigned to the Lake Level districts, as the patient had frequent recurrent attacks of fever during the three months he was in the second Highland district before the attack of "blackwater fever." In my present table this case is credited to the Highlands.

Change of District.—It is a common belief among the older residents

that a change of district, particularly from one level to another, causes "blackwater fever." Many cases have certainly occurred after such a change. The onset varies from a few hours to many days, or even weeks, after the change.

Cases occur in which there has been no change of district for months. Some of the cases are explicable on the ground that a belt of country where the incidence of blackwater fever is high has been traversed. In these cases some days may have been spent on the journey.

In British Central Africa changes of districts are frequent, and it is only a day's journey from the Highlands to a district a few hundred feet above the sea-level, or to one 1500 feet above the sea.

Exposure.—The attacks in a certain number of cases followed unusual exposure. In many cases there was no such antecedent.

"*Blackwater Fever*" *Houses.*—Two houses in particular have this reputation, as there have been several cases of "blackwater fever" in them. On inquiry, however, it is found that some of the cases were brought there with blackwater. The cases have occurred at long intervals, and it is doubtful in both houses if a single case was really contracted there.

Infection.—The disease is not considered to be in any way infectious. Wherever Europeans have settled, cases have occurred, but in no case do they appear to have been even remotely connected with previous cases. In such small groups as have occurred amongst parties of persons, the disease has in some of the instances broken out after the separation, and if dependent on a common cause that common cause was not a previous blackwater fever case.

Certain families seem more susceptible to the disease than others. Thus of one family of three brothers, two had it and died with hyperpyrexia. The third it is stated died with hyperpyrexia without blackwater.

Two other pairs of brothers had blackwater fever. In none of these cases was there any correspondence in the time of the attacks.

Venereal diseases and particularly *syphilis*, are by some supposed to be predisposing causes. Others consider excessive venery as a cause. Instances in support of this can be given, but in a considerable number of cases, including missionaries, such antecedents can be excluded.

Alcoholism can be excluded with even greater certainty. A large proportion of the cases occur in total abstainers. Some of these, as the members, male and female, of the missions, are above suspicion, and in a country where frequent transhipments of goods are required, and where all packages are carried for stages by carriers, any large supplies of alcohol to any of the scattered stations would attract notice and be commented on. Cases do also occur amongst persons known to be intemperate. I have not been able to satisfy myself that these are on the whole either more severe or more fatal.

Drugs.—Much importance has been attached to quinine as a possible cause of blackwater fever. More recently other drugs also, such as phenacetin, have been suspected.

In British Central Africa few persons are without a private stock of drugs. These are frequently abused. With very few exceptions obvious "fever" precedes blackwater, and consequently either quinine, phenacetin, or some other drug is taken. I only know of one case in which no drug had been taken; that was a fairly severe one.

As regards Quinine.—Cases occur in which no quinine has been taken for over a week, and sometimes not for a month before the attack. These cases, as indicated in the attached Chart II, show the same variety in the duration of the hæmoglobinuria, as those in which quinine had been taken.

An exception to this statement might be made as regards my collection of cases, in that amongst those in which quinine had not been taken there are no relapses, and none of the intermittent variety. F. Plehn, however, gives the intermittent form as the common one in non-quinine cases.

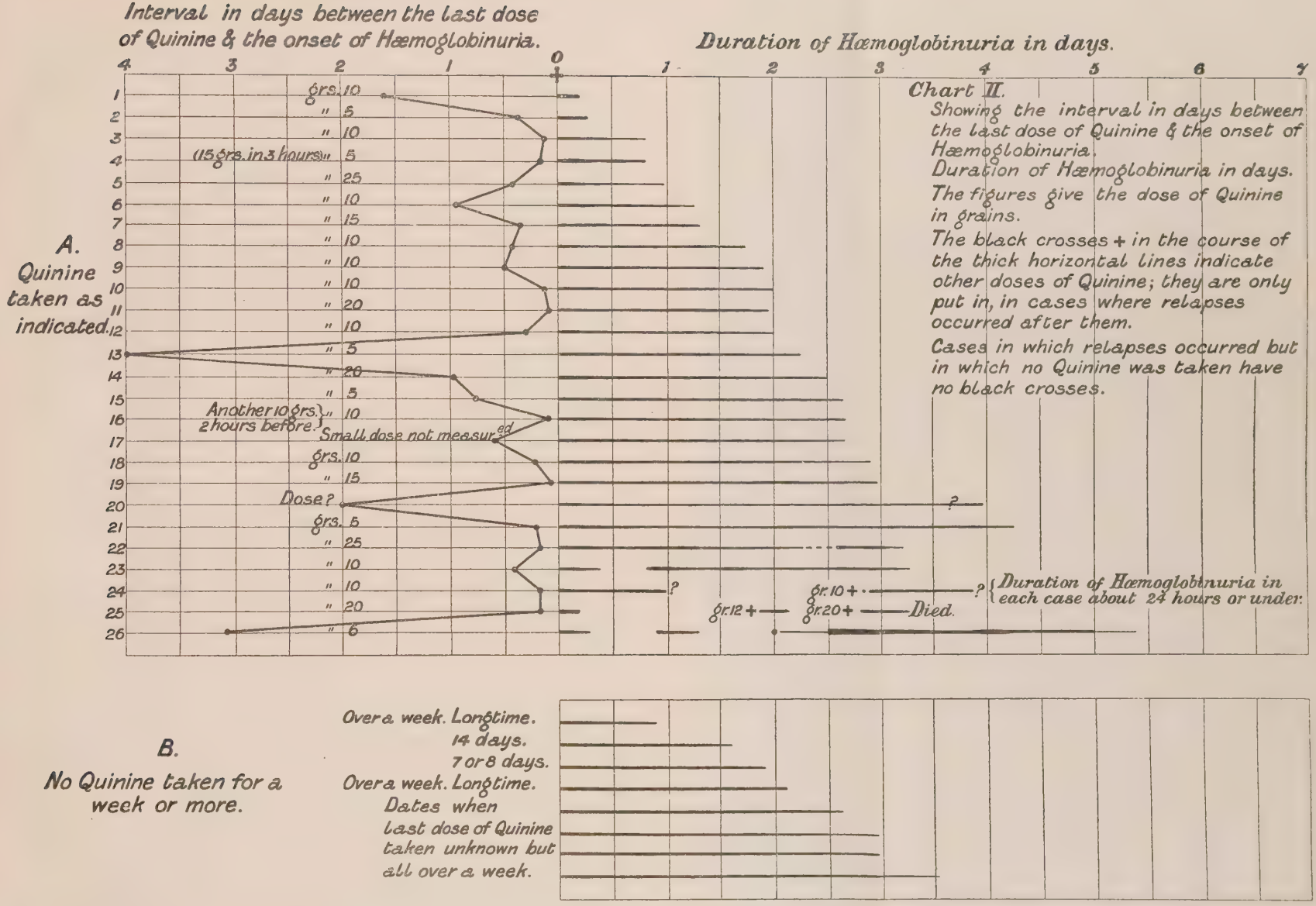
In the cases following the administration of quinine it will be noted that the interval between the last dose of quinine and the onset of the disease is very variable, four days down to one or two hours, and that there is no relation between the amount of the dose and this interval or the duration of the attack.

In several of these cases larger doses were taken both before and after the attack without any hæmoglobinuria following. In cases treated with quinine, sometimes in heroic doses, the hæmoglobinuria ceases, as it does in cases untreated.

These observations show that blackwater fever occurs independently of quinine. In cases where quinine has been taken, to attribute to it a causative action, it must be assumed that this action is independent of the dose, and that the resulting effect is variable, both as to amount and time.

In a few cases there is stronger ground for the belief that quinine is an important factor in the production of the disease. In some a larger dose of quinine has been taken than usual, but, on the other hand, other cases have followed a smaller dose than usual.

In a few cases not only has quinine been taken before the primary attack, but it has also been taken shortly before each relapse, and at no other time. Thus, in (No. 25, Chart II A) quinine, 20 grains, was taken three hours before the attack. The urine cleared in five hours. The next afternoon the patient, contrary to medical advice, again took 12 grains of quinine; hæmoglobinuria again came on in four hours and lasted four hours. The next afternoon, again in opposition to his medical adviser, he took another dose (20 grains) of quinine; hæmoglobinuria for a third time came on in two and a-half hours, and from this


Interval in days between the last dose of Quinine & the onset of Hæmoglobinuria.
Duration of Hæmoglobinuria in days.
4 3 2 1 0 1 2 3 4 5 6 7
A. Quinine taken as indicated.
B. No Quinine taken for a week or more.
Chart II.
Showing the interval in days between the last dose of Quinine & the onset of Hæmoglobinuria.
Duration of Hæmoglobinuria in days.
The figures give the dose of Quinine in grains.
The black crosses + in the course of the thick horizontal lines indicate other doses of Quinine; they are only put in, in cases where relapses occurred after them.
Cases in which relapses occurred but in which no Quinine was taken have no black crosses.
grs. 10
" 5
" 10
(15 grs. in 3 hours) " 5
" 25
" 10
" 15
" 10
" 10
" 10
" 20
" 10
" 5
" 20
" 5
Another 10 grs. " 10
2 hours before.
Small dose not measured
grs. 10
" 15
Dose?
grs. 5
" 25
" 10
" 10
" 20
" 6
?
?
gr. 10 +
gr. 12 +
gr. 20 +
Died.
Duration of Hæmoglobinuria in each case about 24 hours or under.
Over a week. Longtime.
14 days.
7 or 8 days.
Over a week. Longtime.
Dates when last dose of Quinine taken unknown but all over a week.

N.B.—In a few of the other cases it is stated either that they were "not quinine takers" or "no quinine." In the great majority quinine had been taken, and in the majority very shortly before the attacks. These cases are excluded either because the information is insufficient or not quite reliable.

(2.) The *exact* time at which the last dose of quinine was taken and the *exact* time of the onset of hæmoglobinuria, even in the above cases, is uncertain; but for our purposes an error of two or three hours is unimportant.

attack he did not recover. For these particulars I am indebted to Dr. McCarthy Morrough.

Such cases undoubtedly make a strong impression on the observer, but are not conclusive. Similar relapses occur in cases not treated with quinine. In one case (Chart II A, No. 26, and Chart XV) 6 grains of quinine were taken three to four days before the onset of the disease. The urine cleared completely twice, and nearly so a third time. In two other cases there was an intermission (Charts IV and XIV).

The rule in British Central Africa is to take quinine only when the temperature is down in "fever" cases. If this rule had been followed in these three cases quinine would have been taken shortly before each relapse and at no other time. (*Vide* Temperature Charts. The time when quinine would probably have been taken is marked *.)

If quinine had been taken, these cases would have seemed to prove the dependence of the relapses on quinine. In none of the three cases was any quinine taken after the onset.

With so variable a disease as "blackwater fever," statistics are useless, so no comparison can be made between cases treated with quinine and those not so treated. It is not difficult, however, to select cases very similar and running similar courses with and without quinine, and to show that a continuance of the quinine, even in large doses, has no material effect.

For the notes from which these cases are selected I am indebted to Drs. MacVicar, Hearsay, Gray, Cross, Hardy, and others.

Malaria.—The relation of the disease to malaria is certainly not a simple one.

I have made frequent examinations of fresh blood specimens and films in ten cases, and of films only in six more. These films, two or three a day, were sent to me by Drs. Hearsay and Gray in cases I could not attend.

In one only did I find malarial parasites during the period of hæmoglobinuria, and that was about one and a-half hours after the onset, and even in that case no parasites were found at any subsequent examination.

In none of the other cases did I find either malarial or other parasites either during the period of hæmoglobinuria or in the subsequent pyrexial period.

In three cases I had the opportunity of examining the blood before the onset of the disease during the prodromal pyrexia, and in each case "ring" parasites were found. In these cases the parasites had disappeared in the hæmoglobinuria period. In five of the other cases pigmented leucocytes were found, and in two (fatal cases), though no parasites or pigmented leucocytes were found, still at the post-mortem examination the finely-divided pigment characteristic of recent malaria was present in the organs.

These observations show that malarial invasion of a recent date is a common antecedent of "blackwater fever," and that the parasites disappear during the attack. The evidence is against "blackwater fever" being in any way due to an exceptionally numerous invasion.

The suggestion has been made that the parasites are in an internal organ, particularly the brain. The absence of cerebral symptoms in blackwater lends little favour to this hypothesis, and the continued absence of the parasites during several entire cycles from the peripheral blood is, to say the least, unusual. The absence of any marked effect from the use of quinine is also opposed to this view, or to any view which necessitates as an essential a continued malarial invasion.

In three cases I examined the blood during the intermissions (four). In only one of these did I find parasites in small numbers.

These results corroborate in the main F. Plehn's observations in German East Africa. He attributes the disappearance of the parasites to the destruction of them by the altered blood serum. As, however, he and others have observed parasites in some cases during the course of blackwater fever, this explanation is hardly tenable.

If the disappearance or destruction of the parasites, or of some generations of them, is an essential feature of the disease, this destruction may be the cause rather than the effect of the hæmolysis.

In the great majority of cases, blackwater is preceded for one day or more by "fever," indistinguishable clinically from ordinary attacks of malarial fever. As regards its parasitology, this prodromal fever was also indistinguishable in the three cases mentioned above.

To this rule I know of two exceptions. The first is doubtful, as the patient had been feeling "out of sorts" for some time, and in consequence had been taking quinine. He was however able to travel in the usual way by machilla (a hammock) 40 miles, dine in public, and spend the night with friends, who noticed nothing amiss. During the night blackwater fever supervened. It terminated fatally, and the post-morten examination gave pigmentary evidence of recent malaria.

In the second case the onset was very sudden. The patient was, to the best of his knowledge, in good health, and was shooting at a target from his verandah when some abdominal discomfort caused him to go to the latrine, where he found that he was passing blackwater. The case was a fairly severe three days' attack, ending in recovery. There was no medical attendance, and the blood was not examined.

I am not prepared, on the clinical evidence only, of this case to consider it as a conclusive proof of a non-malarial origin. The chief etiological ground for considering "blackwater fever" to be a disease *sui generis*, and unconnected with malarial fever, is the want of correspondence between the seasonal incidence of the two diseases.

In British Central Africa there is no very marked seasonal incidence in either disease, and such as it is, it differs in different districts.

A difference in the seasonal incidence of the two diseases is of little importance, as whatever view may be taken, "blackwater fever" rarely follows a first infection. It usually occurs after several attacks or recrudescences of malaria, and at a variable period sometimes, as in cases occurring in England months after possible infection. This in itself would lead to a seasonal incidence different from that of malarial infections.

The etiological grounds in favour of a malarial origin of blackwater fever are:—

(1) Its prevalence in certain malarial districts. The prevalence in British Central Africa varies with the "prevalence of malaria" in the district, when a correction is made for the varying number of susceptible persons. With further corrections there is a closer correspondence (*vide* Chart III).

(2) Liability to recurrence after considerable intervals, or, though rarely, first attacks of both diseases when the patient is far removed from possible sources of infection. (Note 2, p. 62.)

(3) Diminished susceptibility to both diseases after prolonged residence in an infective district.

With Europeans the common history is much "fever" in the first three or four years; after that, little fever.

With the natives "fever" is common in childhood, and in adult life very rare. A considerable number of these "fevers" have been shown by their parasitology to be malarial.

Enlarged spleens give evidence of malaria usually more or less chronic. The exact relation is unknown.

The age-incidence of this condition in the natives shows a rapid rise and gradual fall, similar to the residential-incidence of "blackwater fever" in Europeans (Chart IV).

The older cases of enlarged spleens, 10–15 years of age, are in the Highland children (10 out of 14), and the majority of those under one year (20 out of 24) at or below the 1,500 feet level. Similarly, the early cases of blackwater fever, those under one year's residence, are mainly (14 out of 21) in persons resident at or below the 1,500 feet level, and the majority (10 out of 14) of those after four years' residence are in persons mainly resident in the Highlands.

(4) If "blackwater fever" is a disease *sui generis* and not of malarial origin, it must also be either a disease originating *de novo*, or originating from some other unknown disease without the characteristic symptoms of hæmolysis and hæmoglobinuria.

Nature of the Disease.—"Blackwater fever" is essentially an acute hæmolysis of sudden onset, short duration, and spontaneous cessation. One of the products of the blood destruction is discharged in quantities with the urine as free hæmoglobin, or more rarely, as methæmoglobin.

It is accompanied by pyrexia, not definitely of malarial or other type. It is usually preceded by pyrexia, and is often followed by a more or less prolonged pyrexia, which may be continued, remittent, or irregular. In occasional cases hyperpyrexia occurs.

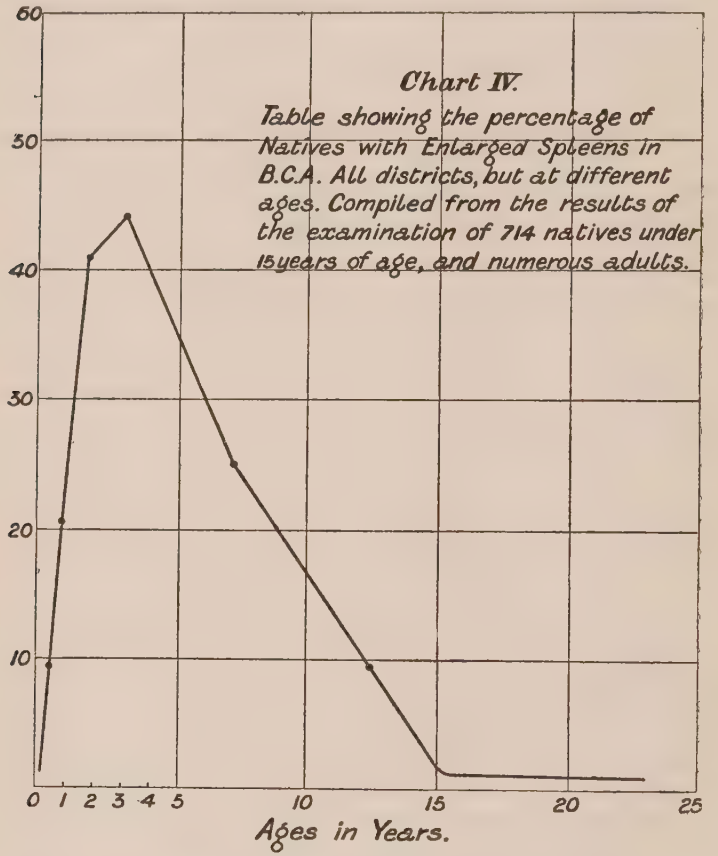


Chart IV.
Table showing the percentage of Natives with Enlarged Spleens in B.C.A. All districts, but at different ages. Compiled from the results of the examination of 714 natives under 15 years of age, and numerous adults.
60
50
40
30
20
10
0 1 2 3 4 5 10 15 20 25
Ages in Years.

The blood destruction is great. In cases where the hæmoglobinuria lasts for over two and a-half days, the number of red corpuscles fell to 1,038,000, 1,290,000, 1,366,000, and 1,680,000 respectively, from presumably little below normal.

Even in shorter cases, lasting about twenty-four hours, there is fall to below 3,000,000. In some cases at least, the hæmoglobin is more reduced than the corpuscles.

The prodromal pyrexia has not been much studied, as cases rarely come under medical observation at this stage, and even when they do, they are not recognised as blackwater at this period. During this stage rigors are unusual, and not marked. In this they resemble

ordinary malarial attacks in British Central Africa. During the hæmoglobinuric period severe rigors are the rule; they are often initial, but may be later. Sometimes there are repeated rigors. Complete absence of rigor is rare, but does occur.

With the cessation of the hæmoglobinuria there is usually a fall in the temperature sometimes to subnormal. These changes and the subsequent pyrexia are illustrated by the Temperature Charts.

Shortly after the onset of the disease the conjunctivæ and skin show an icteric tinge closely resembling jaundice. In such cases as I have seen there has been no bile pigment in the urine. There can be little doubt that this colour is derived from the blood pigment. This coloration may be intense, especially in suppression cases.

The condition of the skin varies, but as a rule there is profuse diaphoresis even when the temperature is high. It is frequently intermittent.

The pulse-rate is not much raised considering the temperature, and in cases I have seen has been about 90, rarely up to 100. In other cases noted here it has sometimes been much higher.

As the anæmia advances the pulse usually becomes dicrotic. Respirations also become more frequent; 28—32, whilst keeping still, are not uncommon.

The severity of the disease varies greatly according, 1st, to its duration, and 2nd, as regards complications. The duration, when there are no relapses, varies from a few hours up to, as a common period, rather under three days. Some observers consider the last as the common type. Cases in which the hæmoglobinuria persists longer than three days are rare without either partial or complete intermissions.

There seems no reason to attempt to distinguish separate forms of blackwater fever. Intermediate forms occur as regards duration or any single symptom. Such divisions as "quinine form," "bilious" forms, &c., may be misleading and cause confusion.

Relapses are common. They may occur before the urine is quite free from hæmoglobin, in which case the hæmoglobinuric period may be much over three days. They commonly occur after the urine has been clear for a few hours, and more rarely after several days or even two or three weeks' intermission. There does not seem to be any definite relation between the primary attack and the relapses as regards duration. The first attack may be a short one, and the relapses long, or *vice versa*, or they may be each of about the same duration. (Charts II A, 22 and 23, and Temperature Charts IV, XIV, and XV illustrate this condition.)

Vomiting is a common symptom and is frequently severe and persistent. When excessive the prognosis is unfavourable. In rare cases there is either no or very little vomiting.

Hiccough is very common. It occurs in mild as well as in severe cases, and unless excessive is of no prognostic import.

Hæmorrhages are not a usual feature of the disease, but occur in some cases. The commonest form is epistaxis, but in two there was hæmatemesis and in one hæmorrhage from the bowel.

Glandular enlargement was noted in three of the collected cases, in each case in the neck. In one of these cases there was extensive suppuration, terminating fatally. In some cases of malaria there is glandular enlargement.

Gastro-enteritis with dysenteric symptoms appears to have occurred in several cases. This I have not seen.

The mortality of the disease is variously given. It is probably overstated as a rule. There is a tendency to report all deaths, when there has been no doctor in attendance, as "blackwater fever." On the other hand, cases that recover from what appears to have been "blackwater fever," in the absence of medical testimony, are doubted. The fatal cases are remembered whilst the recoveries are forgotten. For these reasons I consider that the figures given below exaggerate the gravity of the disease.

In all, I have collected some accounts of the disease in 136 persons from the district. Amongst them they had 184 attacks.

Of the 136 first attacks	31 or 22·7	per cent.	were fatal.
„ 33 second attacks	8 or 24	„	„
„ 15 third or fourth attacks	2 or 13·3	„	„

In this variable disease the mortality is no guide to the success of the line of treatment adopted. In the cases of a few hours' duration deaths are rare; in those lasting over two days deaths are common. A collection including a large proportion of short attacks will give a low mortality; whilst a series in which few of these mild cases are included will give a high mortality.

In British Central Africa some of the medical men seem to have seen little of the milder forms till this year, but they have occurred for many years past.

The supposition that the milder forms are on the increase, like the statement that "blackwater fever" itself is of recent appearance, is not, I think, warranted by the facts known.

The increased European population, greater facilities for travel, and the larger number of medical practitioners have enabled a larger proportion of the cases to be seen, and that at an earlier stage. The attention directed to the disease has led to cases being recorded which otherwise would have been speedily forgotten.

There are three main causes of death—suppression of urine, cardiac, failure, and hyperpyrexia.

Of these, suppression is the commonest. This is rarely complete,

though the amounts passed may be very small, and at the rate of only a few drams daily.

I have not seen this complication. From notes supplied to me by Drs. Gray and Hearsay, we find that in one case 7 ounces of urine were passed in five days; in another, 8 ounces 1 dram were passed in five days; in another 2 drams in two days, and in another 25 ounces were passed in the first twenty-four hours of the disease, and only $10\frac{3}{4}$ in the whole of the remaining nine days.

It is noteworthy that, in spite of the small amounts of urine passed, not only does it become free from hæmoglobin, but even that it may be free from albumen. This shows that the products of the hæmolysis, failing a passage by the kidneys, are removed in some other way (Note 3).

In cases of blackwater fever terminating in recovery the amount of urine passed is variable. Whilst there is much hæmoglobin the amount passed is usually much above normal. As the urine clears it falls below normal and may remain below for days or only for a brief period. This variation takes place even in the milder cases. Urine Charts A (1), (2), (3), and (4) illustrate this condition.

Suppression usually occurs when the urine is commencing to clear, and this drop may be taken to indicate a tendency towards it. The hæmoglobinuric urine appears to act as a diuretic. There is evidence, however, that it acts as an irritant on the genito-urinary tract.

Micturition is frequent; sometimes urine is passed every hour or even more frequently. This is particularly so during the second day.

At this time much bladder epithelium is found in the urinary deposit. Dysuria and tenesmus are rare but occur. There is discomfort, rarely amounting to pain in micturition, and in two cases there was actual retention. Retraction of the testicles is common. These symptoms disappear as the urine clears.

It is tempting to attribute the suppression to mechanical causes. There is little evidence of any important structural change in the kidneys. With the disappearance of the hæmoglobinuria there is a great fall in the amount of albumen, and usually in a day or two and sometimes even after the first micturition none at all is found. Casts persist longer, and an occasional one may be found weeks after the attack.

The symptoms associated with this suppression are not those of uræmia. Consciousness is maintained till near the end; convulsions are very rare and even muscular twitchings are unusual. Vomiting is usually marked. The temperature is often subnormal. (Note 4.) Temperature Chart 12 is that of a suppression case reported by Dr. Gray, P.M.O., British Central Africa.

A temporary suppression could be accounted for, when it occurs early, by the irritation set up by the hæmoglobinuric urine; and the

late cases by the combination of the fall of the blood pressure, the anæmia and the cessation of the excretion of diuretic constituents of the urine (hæmoglobin), but neither of these sufficiently explain the persistence of the suppression.

They might explain the commencement but not the continuance.

The accumulation of pigment (yellow) and of ferruginous materials in the liver, as found post-mortem, indicate the alternative method of eliminating the hæmolytic products from the blood.

Cardiac failure is common. It has in several cases been the cause of death as a result of slight exertion.

Hyperpyrexia is not common, though pyrexia is often severe. In the cases of which I have notes, it occurred after the hæmoglobinuric period. It does not seem to be controlled by quinine or antipyretics (Temperature Charts 10 and 11).

Second attacks are common. Of the 136 patients, 33 are known to have had two or more attacks, 24 per cent. As many persons leave after one attack and do not return, this probably understates the liability. The longest interval between the first and second attack is nine years. It is often less than one year. Second attacks under a month would be considered as relapses.

The health between the two attacks is usually good.

F. Plehn states that the mortality is greatest in the first attacks. My returns are not sufficiently numerous to justify any decided conclusion, though the actual figures indicate a slight increase in the mortality in second attacks and a decreased one in subsequent attacks.

In some persons each attack resembles the first. Thus one person has had three attacks each lasting only a few hours, another had two attacks within a year, each lasting just under two days, and a third two attacks, each lasting two and a half days.

This is not an invariable rule, as one person whose first attack lasted under twenty-four hours had his second attack nine years after, which lasted a full three days.

This tendency to persistence in type of the disease in an individual perhaps accounts for the absence of a markedly increased mortality with later attacks.

A severe first attack is fatal, or the person permanently leaves the country. Second attacks will, in the majority of cases, be in persons who had slight or only moderately severe first attacks, and as far as the type remains the same will have slight or moderately severe second attacks.

Treatment.—The popular belief in an excessive mortality from "blackwater fever" has led in the past to somewhat heroic treatment. The rapid course of the disease, with the progressive failure in strength, has resulted in frequent changes in treatment before any one method has had a sufficient trial.

Errors as to the true nature of the disease have been common. By some it seems to have been considered as a hæmorrhage, and hæmostatics, such as ergot, perchloride of iron, &c., have been freely resorted to, not only by the mouth or hypodermic injections but also by intra-renal injections.

Restriction of fluids seems to have been advocated by some partly for this reason, but mainly with the idea of checking vomiting. Quinine has been very freely used by some, subcutaneously and otherwise.

Comparisons of the mortality under different treatments is useless on account of the varying severity of the disease.

Judging from individual cases I have seen under various methods of treatment, and comparing them with notes of other cases supplied to me, I do not think that any treatment hitherto employed has the slightest influence on the duration of the hæmoglobinuria or hæmolysis.

From the depth of colour of the urine passed in the early stages, the duration of the attack can be fairly correctly estimated, unless relapses occur, irrespective of treatment.

Parallel cases, with or without quinine or any other specified drug, can be easily found. Alteration or cessation of a treatment does not make any material difference.

Quinine has little or no effect on the temperature, and antipyretics, such as phenacetin, have so temporary an effect, sometimes followed by a greater rise, that I consider their use doubtful and their repeated use dangerous (*vide* Temperature Chart 4).

Whatever the connection with malaria may be, I think quinine should be avoided unless there is direct evidence of *present* malarial infection as shown by finding parasites. Even when parasites are present, I should be inclined to use it with caution, as it increases the vomiting, and in large doses causes much depression.

The treatment, therefore, is necessarily *symptomatic*. The chief danger is, or is heralded by, suppression, and consequently diuretics have been extensively used.

Terebene, introduced by Dr. Kerr Cross, has been extensively employed, and a considerable number of cases so treated have recovered. In the cases I saw, no effect seemed to follow its use or disuse. In cases of suppression, no rise in the amount of urine has followed its administration. Considering the signs of genito-urinary irritation present in the blackwater stage, a less irritant diuretic would appear to be indicated, but I cannot say that I have seen ill-effects follow its use. In some cases it is said to cause vomiting. Non-irritating diuretics have also been freely used, and recoveries have been numerous.

The simplest form is, perhaps, that of taking large amounts of fluid —plain water, soda water, lemonade, &c.

A treatment frequently practised in the past year was Sternberg's treatment for yellow fever; this was introduced by Dr. Hearsay. Frequent doses of bicarbonate of soda, with minute doses of perchloride of mercury, are given. In some eleven cases so treated there has been little vomiting and no suppression.

It is, in my opinion, worthy of a fuller trial, and is quite harmless. It has not yet been fully tested by a suppression case. It can only be considered as a symptomatic treatment.

In cases where the vomiting has been persistent, morphia has been used hypodermically.

Sulphonal checks the restlessness so common in the disease. No ill-effects have been observed.

Most practitioners make a strong point of "feeding up" the patients, particularly with various meat extracts; they are not necessary, and, considering the large amount of waste products to be excreted, may be injurious. One patient, who recovered from a severe attack, treated himself on lime juice and soda water in large quantities, but had no food at all, "not even milk." In a severe case, stimulants are required later on; too early a resort to them is to be deprecated.

Prophylaxis.—Till the origin of the disease be known it is useless to discuss the question. If the views I hold be correct, it would be bound up with the prophylaxis of malaria. Comparisons between "blackwater fever" and various other diseases have been made.

Yellow fever resembles it in that there is a similar racial susceptibility and immunity, in the variability of the severity and duration of the disease, in the unfavourable prognosis with excessive vomiting, and the fatal augury of suppression.

Apart from bacteriological grounds, blackwater fever is distinctly separated from yellow fever by not being contagious or occurring in an epidemic form.

Paroxysmal hæmoglobinuria has merely the resemblance that hæmoglobin is present in the urine in both. Any attempt to otherwise compare the two fails.

For etiological purposes it is unimportant, as paroxysmal hæmoglobinuria is a disease of great rarity, not markedly more common in the tropics than elsewhere, whilst "blackwater fever" affects a *considerable percentage* of the European population under varied climatic conditions in malarial districts of Africa alone. It occurs but only rarely in other malarial countries, India, British Guiana, West Indies, &c.

With anæmias, including malarial anæmia and cachexias, it has the differences of its short duration, rapid course, and uniform tendency to speedy recovery, unless complications terminating fatally arise.

If kala azar be taken as the type of the malarial cachexia, it would be a secondary fever due to, or accompanied by, chronic visceral changes persisting after the malarial invasions had subsided. Black-

water fever, if a malarial origin were admitted, would have to be considered as a secondary disease characterised by acute temporary hæmolysis, not associated with causative visceral changes, but originating with an abrupt subsidence of a malarial invasion.

With ordinary forms of malaria, including the comatose one, there are no analogies at all.

The nearest perhaps is the "algide" form. In exceptional cases of blackwater fever the onset has been with marked collapse and continued prostration, whilst the urine has not contained large amounts of hæmoglobin. Such a case might be considered as an intermediate form.

In the present state of our knowledge of the disease opinions are of little or no value. The weight of evidence is in favour of a malarial origin. The character and parasitology of the prodromal stage appears to me to be the important period, and is not likely to be worked out till blood examinations in cases of malaria become a routine.

In conclusion, I consider that the balance of evidence is in favour of the view that "blackwater fever" commences in individuals suffering at the time from an invasion by the malaria parasites; but that there is no evidence to show that the attack actually depends on an exceptionally large number of these parasites, an exceptional degree of anæmia or visceral alteration, or on climatic influences or the exhibition of drugs.

What actually determines an attack of "blackwater fever" I am not in a position to state. Before the problem can be solved much more information is required regarding the period immediately preceding the onset of the attack, especially in connection with the parasitology and condition of the blood at that period.

Such data are peculiarly difficult to ascertain, as there is no known means of diagnosing the disease in the prodromal period.

The whole question of malarial sequelæ, including secondary fevers and the causation of visceral changes, requires more investigation, as it has been comparatively neglected since the knowledge of malarial parasitology became general.

The mode of production of immunity, temporary and persistent, is as yet unknown, and also requires much more study.

"Blackwater fever" may be due to some derangement or interruption of such processes, and therefore in our present state of knowledge it is futile to theorise.

Certain manifestations of malaria appear to be more common in some malarial countries than in others, though the parasites appear to be indistinguishable.

It is possible that these differences may depend on the different definitive hosts of the malaria parasites.

Several species of Anopheles have been proved to carry the malaria parasites. Mr. F. V. Theobald has identified three of the Anopheles found in British Central Africa as three found on the West Coast of Africa; but one, *A. paludis* (Theobald), is in the form of a distinct variety. These mosquitoes have not been found in other countries.

If the prevalence of "blackwater fever" in Africa is due to one or all of these hosts, *Anopheles funestus* must be one of those implicated.

A knowledge of the exact geographical distributions of the various species of malaria-bearing Anopheles is required in this connection, as well as the geographical distribution of "blackwater fever" and of special manifestations of malaria.

Notes.

1. The natives of British Central Africa have the woolly hair of the negro. The features are coarse but not typically negroid, and there are considerable tribal and individual variations in this respect. They are of various shades of colour from brown to black.

The tribes I have had most dealings with are the Yao, Manganja, and Angoni. There is a slight Arab admixture in some districts, and a larger Zulu in others. As a whole they belong to the Bantu division of the African races.

2. Two cases of "blackwater fever" have occurred in persons after arrival in England who had never had blackwater fever during their residence in British Central Africa. They had both had ordinary "fever" in Africa.

3. In early "suppression cases" the anæmia and icterus continue to increase although little or no hæmoglobinuric urine is excreted. The case (Chart 12) under the care of Dr. Gray is the only one I know of in which the number of corpuscles was estimated. Suppression set in within twenty-four hours of the onset of the disease. The number of corpuscles, as determined by Dr. Gray was 3,170,000 on the first day, 2,360,000 on the second, 2,180,000 on the third, and 1,740,000 on the fourth day. During the second, third, and fourth days a total of 4 ounces of urine was passed. The estimates for the next two days were 1,800,000 and 1,630,000 respectively. Suppression continued till death on the tenth day.

4. There appears to be considerable variation in the symptoms associated with suppression in "blackwater fever." In occasional cases, as in some of the suppression cases in yellow fever, the patient is perfectly rational and conscious just before death. The cerebral symptoms that occur are drowsiness, irritability, and sometimes mental weakness or confusion. Delirium during sleep is common. Convulsions are very rare. Coma only occurs, and not always even then, shortly before death. Life is usually prolonged for three or four days after the onset of suppression, but may be as long as nine days.

There is, as a rule, little disturbance of the special senses, though loss of vision has been complained of. The pupils are in some cases dilated. Deafness is common only in cases treated by quinine.

There is steady loss of muscular strength in most cases, but not in all. Muscular twitchings are usually absent, even to the last. As a rule there is much vomiting, and often hiccough.

Occasionally a "uræmic smell" has been noted, but this is not usual. Anasarca does not occur. The urine may be free from albumin towards the end.

ILLUSTRATIVE TEMPERATURE CHARTS (pp. 64–77).

Chart 1.—"Blackwater fever." Mild attack. Prodromal period taken for ordinary malarial attack, and parasites found.

Onset without rigor.

Post-hæmoglobinuric pyrexia.

The charts in three previous attacks of malaria and one subsequent attack attached.

,, 2.—"Blackwater fever." Severe attack. This followed repeated attacks of fever for a period of three months.

The day before the attack "fever" taken to be ordinary malaria. Parasites found in fair numbers.

No complications. Post-hæmoglobinuric pyrexia very slight.

,, 3.—"Blackwater fever." Severe attack.

Prolonged and severe post-hæmoglobinuric pyrexia not markedly affected by quinine in considerable doses.

,, 4.—"Blackwater fever." Severe attack.

Prolonged and severe post-hæmoglobinuric pyrexia.

Treatment mainly by phenacetin. Temporary effect of this drug followed in some instances by a higher rise.

In this case there was an intermission in the hæmoglobinuria, during this intermission parasites were found.

Quinine *not* given during the intermission; if it had been it would, according to custom, have been given when the temperature was down only (*), *i.e.*, in this case about five hours before the relapse.

5.—"Blackwater fever." More continuous form of post-hæmoglobinuric pyrexia.

,, 6.—"Blackwater fever." Mild attack.

No post-hæmoglobinuric pyrexia.

,, 7.—(Indian) "Blackwater fever." Patient was under treatment for enlarged spleen, anæmia, and chronic "fever," secondary malarial fever (?).

Unusually slight pyrexial disturbance, either before, during, or after the hæmoglubinuric period. I can find no record of a case similar in these respects.

8.—"Blackwater fever." Medium severity. Prodromal period not marked by definite illness, as patient was able to live an ordinary life. Temperature was taken night before the attack and found to be raised, 105° F.

Post-hæmoglobinuric pyrexia moderate. Very little treatment. Good effect of an occasional dose of phenacetin (?).

Chart 9.—"Blackwater fever." Two attacks in same person at an interval of four months. Good health in between.

Last attack came on about eight days after last dose of quinine.

Second attack came on about twelve hours after last dose of quinine.

Charts 10 & 11.—"Blackwater fever." Attacks not severe, but *hyperpyrexia* in post-hæmoglobinuric period.

Chart 12.—"Blackwater fever." Suppression of urine. Fatal.

Followed untreated malaria. No quinine taken for a fortnight. Post-hæmoglobinuric pyrexia appears to be rare in suppression cases.

,, 13.—"Blackwater fever." Severe case followed by acute lobar pneumonia.

No definite marked prodromal period. Malaise only. Temperature not taken. Post-mortem showed pigment disposed as in recent malaria.

,, 14.—"Blackwater fever." Relapse occurring on the third day before the urine had quite cleared.

According to the usual local rule for the administration of quinine, it might have been taken on the morning of the second day, but more probably would not have been taken till the third day, in which case the relapse would have been attributed to the quinine. None was taken.

,, 15.—"Blackwater fever." Series of relapses. The early ones of short duration and methæmoglobin only in the urine. The final attack was hæmoglobinuric and came on before the urine was quite free from methæmoglobin. Hepatic pain a marked feature, both of the early attacks and also in the rises of temperature in the post-hæmoglobinuric period.

Quinine, according to usage, would have been taken on the second and third days (*), and the relapses then would have been attributed to it. None was taken.

Probably the patient's temperature was also down on the first day of the chart, as he was out.

In this case there was hardly any vomiting.

(a) DISEASE

Malarial Fever.

NOTES OF CASE

Chart 1.

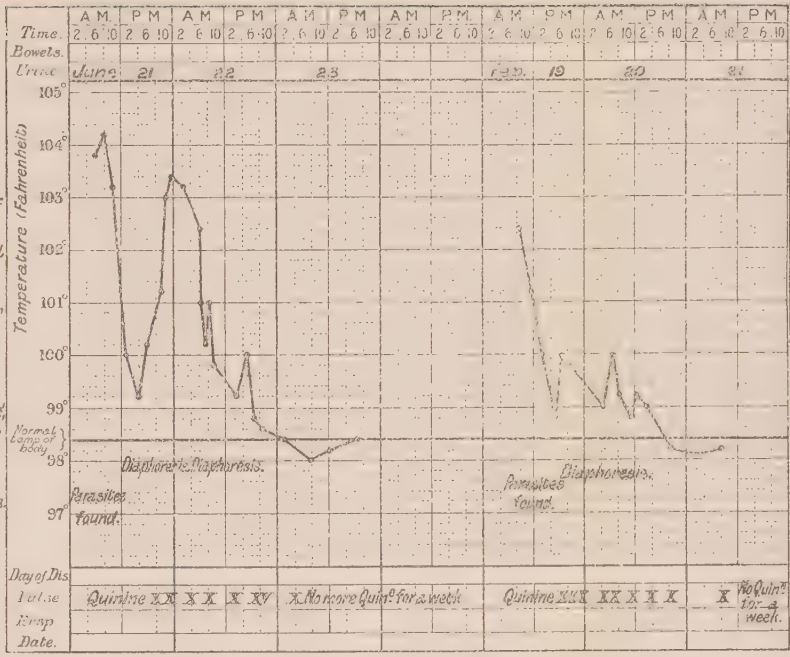
10th, 11th, & 12th, attacks of Malarial Fever, terminating in recovery without unusual symptoms.

13th attack & during its course "Blackwater Fever."

A subsequent Pyrexial Fever non-malarial.

14th attack of Malarial Fever, one cycle untreated, the second treated with Quinine.

No definite subsequent attacks in next 5 months.


Time.
A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M.
2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10
Bowels.
Urine.
June 21 22 23 24. 25. 26 27 28
105°
104°
103°
102°
101°
100°
99°
Normal Temp of body
98°
97°
Temperature (Fahrenheit)
Diaphoresis. Diaphoresis.
Parasites found.
Parasites found. Diaphoresis.
Day of Dis.
Pulse
Resp.
Date.
Quinine XX X X X XV X No more Quin.e for a week Quinine XXX XX X X X X No Quin.e for a week.

(c) DISEASE

Blackwater Fever

1st attack.

Name D.

NOTES OF CASE

Frequent short attacks of fever in previous 11 months all treated energetically with Quinine.

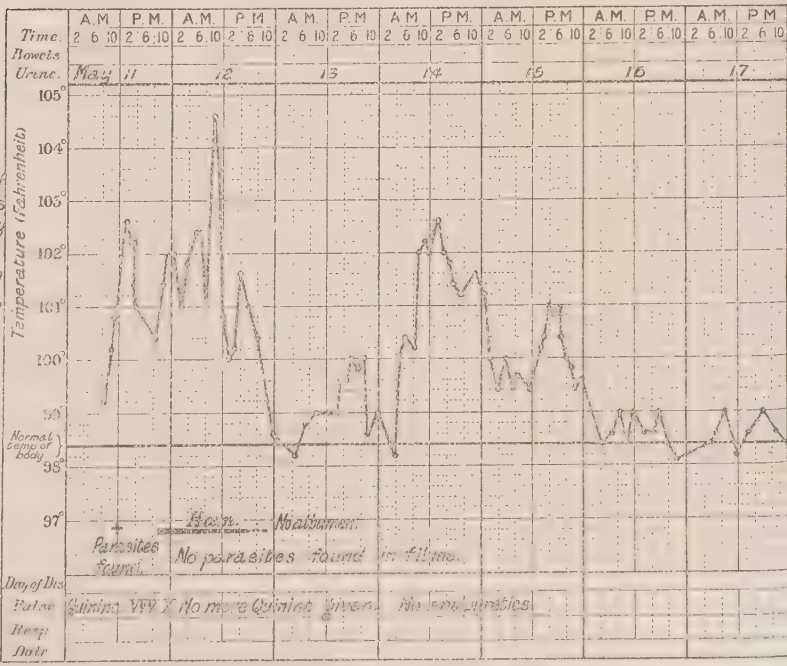
Last attack of "Fever" March 23th. An interval of 7 weeks, the longest since June.

Health in interval fair, considerable lassitude & want of appetite, but Temp. never found to be above normal.

Quinine gr. X. two days before onset of "Fever."

Onset of "Blackwater" with severe abdominal, not renal pain. Relieved by induced vomiting. No rigors.

RESULT Recovery.


Time.
A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M. A.M. P.M.
2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10 2 6 10
Bowels.
Urine.
May 11 12 13 14 15 16 17
105°
104°
103°
102°
101°
100°
99°
Normal Temp of body
98°
97°
Temperature (Fahrenheit)
Parasites found.
H.w. No albumen.
No parasites found in film.
Day of Dis.
Pulse
Resp.
Date
Quinine XVV X No more Quinine given. No malignancies

(b) DISEASE

Malarial Fever.

NOTES OF CASE

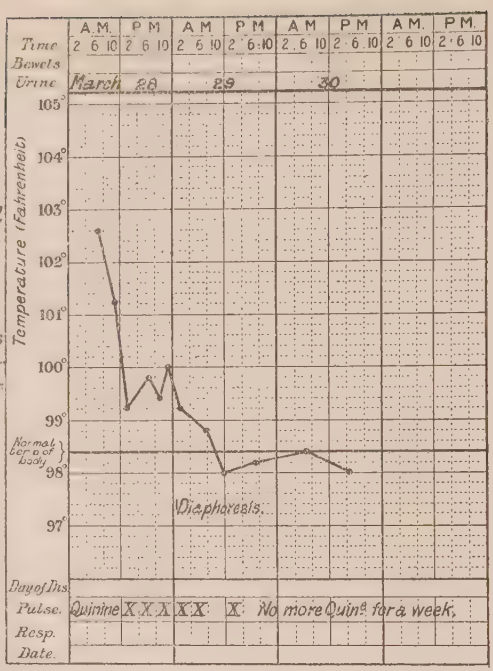
Travelling. Quinine grs. XV had been taken March 25th.

Had been in good health since last attack of fever Feb. 13th.

Temperature had been taken two or three times a week & blood examinations made, with negative results.

Quinine X or XV grains every 5 days and an occasional other dose.

"Fever" came on in the night. No films taken.



(d) DISEASE

Malarial Fever, 16 days after "Blackwaer."

NOTES OF CASE

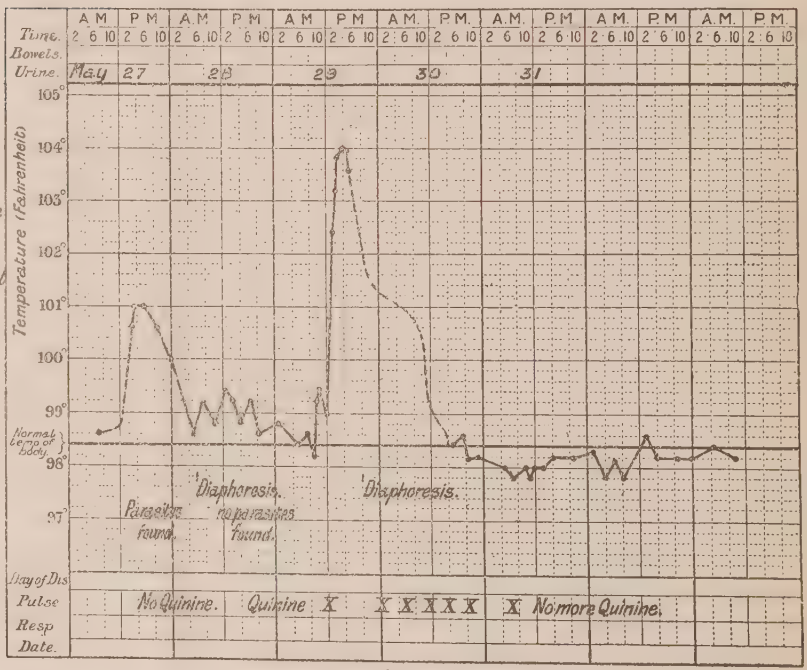
Temperature taken daily, & frequently two or three times a day since May 17th. Once or twice 99°F., but usually normal or slightly sub-normal.

No Quinine taken.

Last Blood Examination 2 days before. Negative.

Parasites found at onset of fever, none 2nd day.

Third day not examined.



DISEASE.

Blackwater Fever
1st attack.
Under care of Dr Hearsay.
Name. W.
Age. 27.

NOTES OF CASE.

Chart 2.

First had fever three months ago, since then has had it about every other week.
Had 3 days fever 12 days before, and the 2 days before this attack.
Has taken 250 grs. of quinine in the 3 months, but never as much as 20 grs. in a day.
Treatment after onset, Sodium Bicarbonate & Lig. Hydrarg. Perchlor.
Herpes Preputialis during convalescence.
Was free from "fever" for some weeks after the attack.

RESULT Recovery.

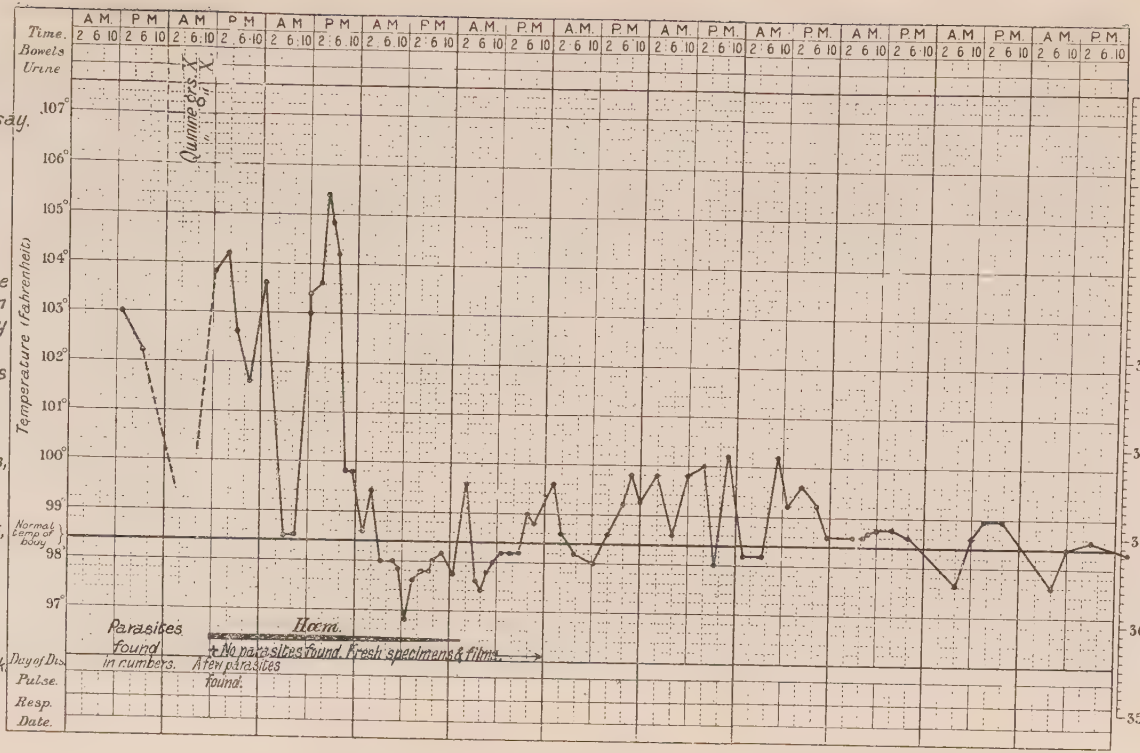


Chart 3.

DISEASE

Blackwater Fever
1st attack.
Name A.
Under the care of
Dr. MacVicar.

NOTES OF CASE

"Fever" for 3 days previous.
Temperature the day before 105°F.
Had fever for 2 days, a week ago.
In this case quinine was given freely, and patient recovered; but not only did the temperature rise whilst full doses were taken, but did not fall for several days.
The duration of Hæmoglobinuria is uncertain. It was "clearing" on the morning of 4th day.

RESULT Recovery.

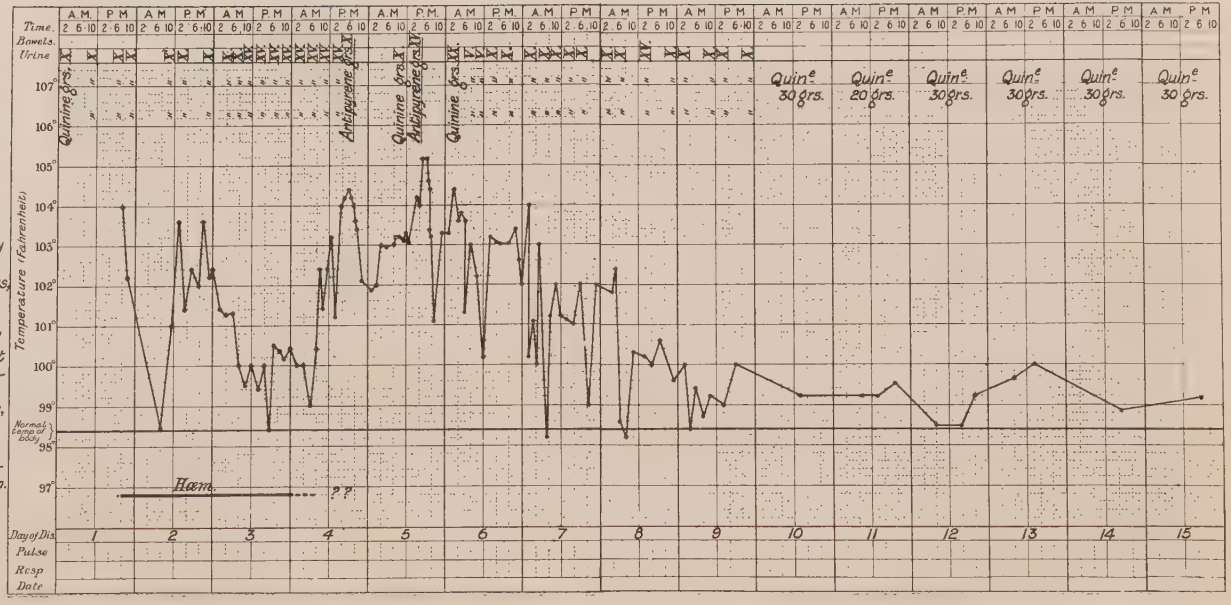


Chart 4.

DISEASE

Blackwater Fever 2nd attack.

Under the care of Dr Hearsay.

Name O.

NOTES OF CASE

Previous attack eleven months before.

Had enjoyed good health between the attacks.

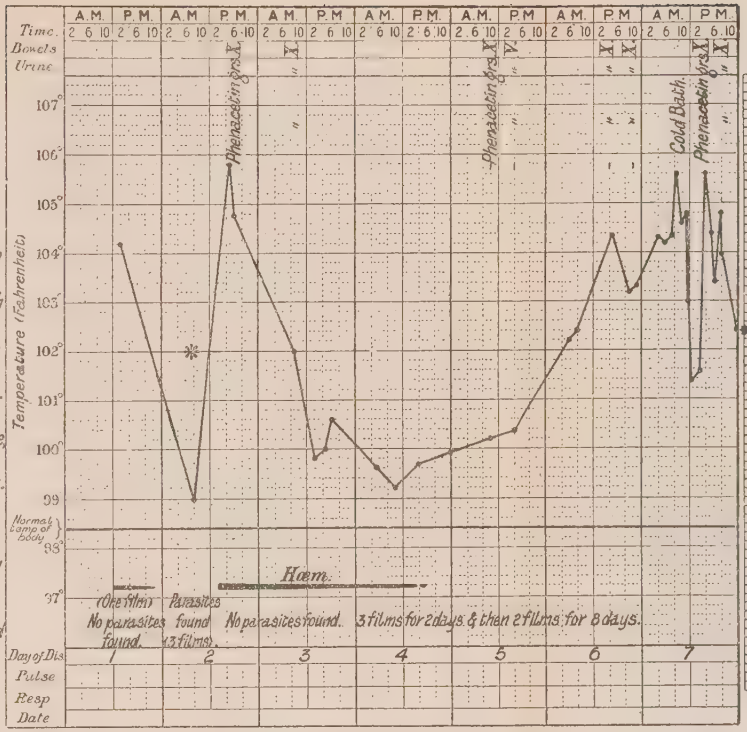
For three days before this attack, was unwell & had much headache. Was able to get about.

Had taken some quinine the last dose (10 grs) the even before the attack.

Films during the first attack, no parasites.

Three films during the intermission, all showed parasites. In the last, noon 2nd day, only one was found & that showed signs of early sporulation.

RESULT Recovered.



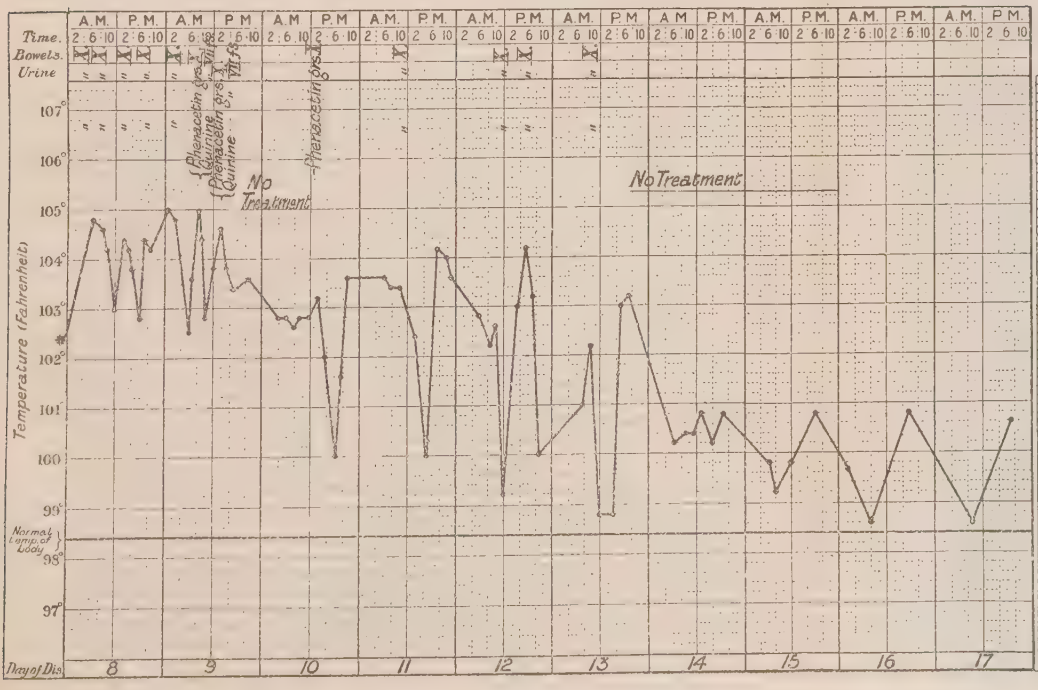


Chart 5.

DISEASE

Blackwater Fever
2nd attack.

Name M.

Under care of
Dr Laws.

NOTES OF CASE

Showing more continuous type of Post Hæmoglobinuric Pyrexia.

In addition to treatment on chart, Morphia Ergotine & 15 minim doses of Perchloride of Iron were given.

Constant feeding and free stimulation.

RESULT Recovery.

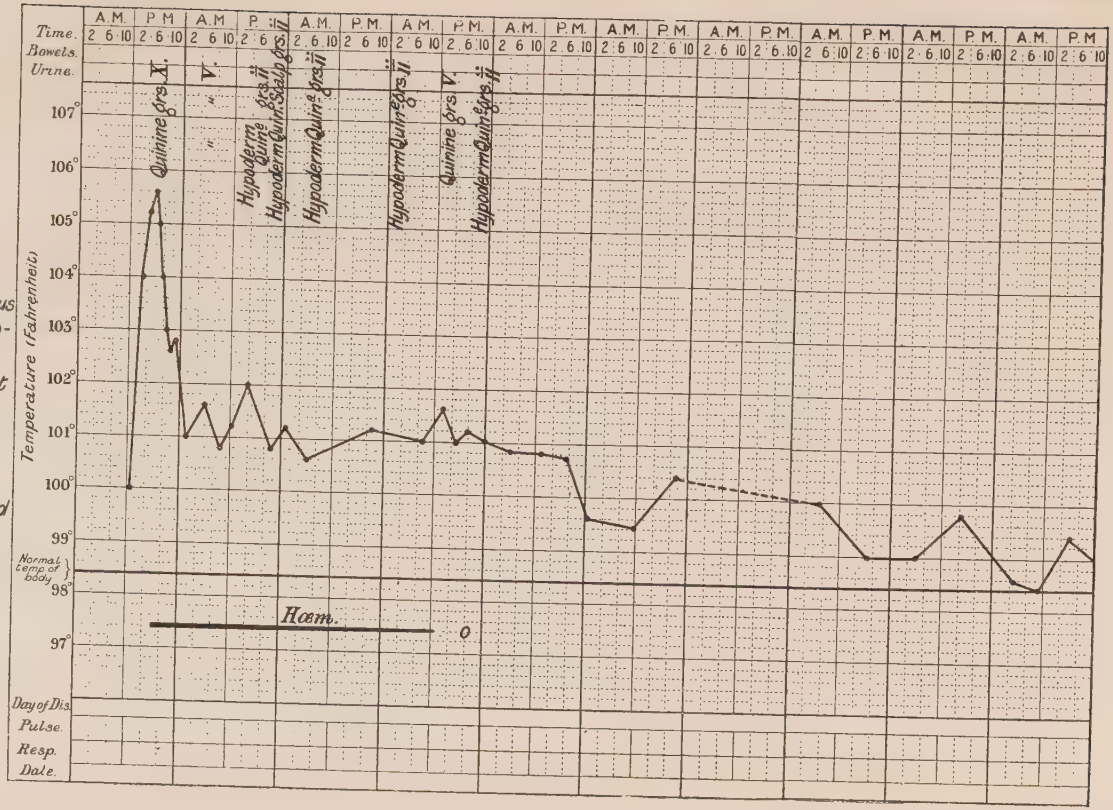


Chart 6.

DISEASE

Blackwater Fever
1st attack.

Name B.
Under care of
Dr Kerr Cross.

NOTES OF CASE

2½ years B.C.A.
Had been having fever off & on for 10 days with much vomiting.
Was taking quinine 15-30 grs. in a day, but not continuously.
Had temperatures of 101°F. on the 2 days before the attack.
No definite rigor at onset but one about 10 hours after.
No complications but convalescence slow.
Had crescent about 12 days after. No parasites found in attack.
RESULT Recovery.

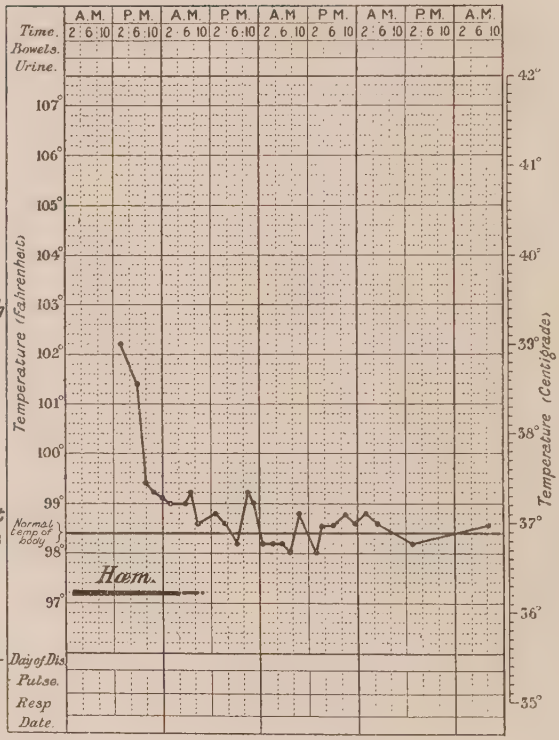


Chart 7.

DISEASE

"Blackwater Fever"

Name C.S.

Under the care of
Dr Hearsay.

NOTES OF CASE

Sikh. Anæmia and enlarged Spleen.

The case is remarkable for the very slight disturbance in temperature during the period of Hæmoglobinuria.

There was low continued fever before, during, & after the Blackwater.

No parasites found in films taken during & after the Blackwater Period.

Treatment:–

Bicarbonate of Soda & Lig. Hyd. Perchlor.

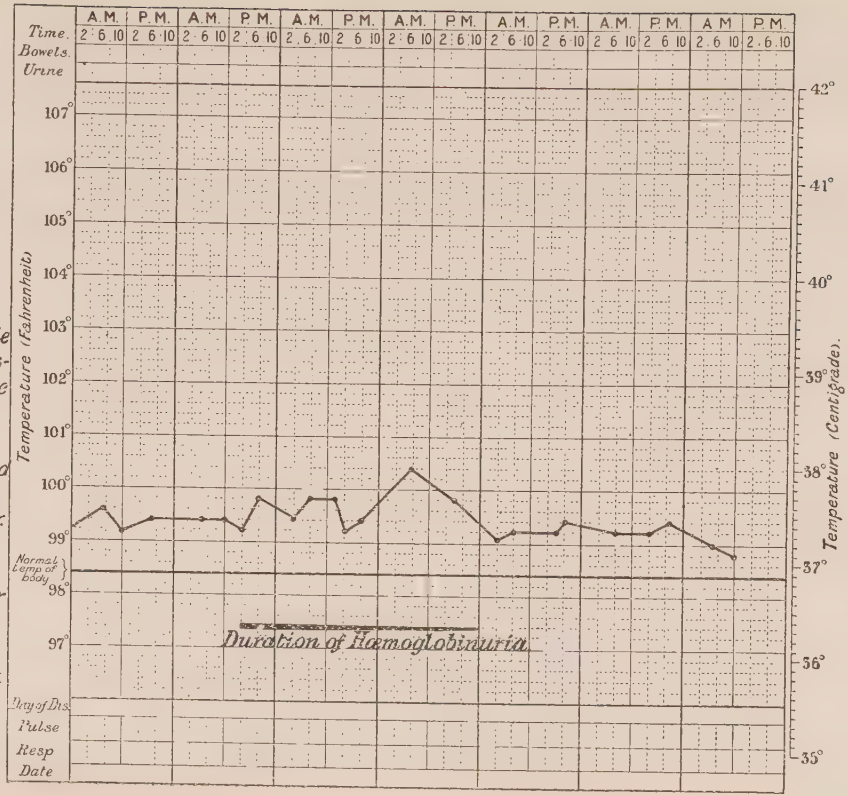


Chart 8.

DISEASE

Blackwater Fever
1st attack.

Name C.
Under the care of
Dr Hearsay.

NOTES OF CASE

Had been having "fever" off & on for some time. Resident in Shire Highlands & only left there 2 days before attack. Appeared in fair health day before attack, but at night his temperature was up & he took X grs. quine. Rigor initial. Moderate vomiting.

Treatment:–
Sodium Bicarbonate, & Lig. Hydrarg. Perchlor.
No parasites found. Pigmented Leucocytes.

RESULT Recovery.

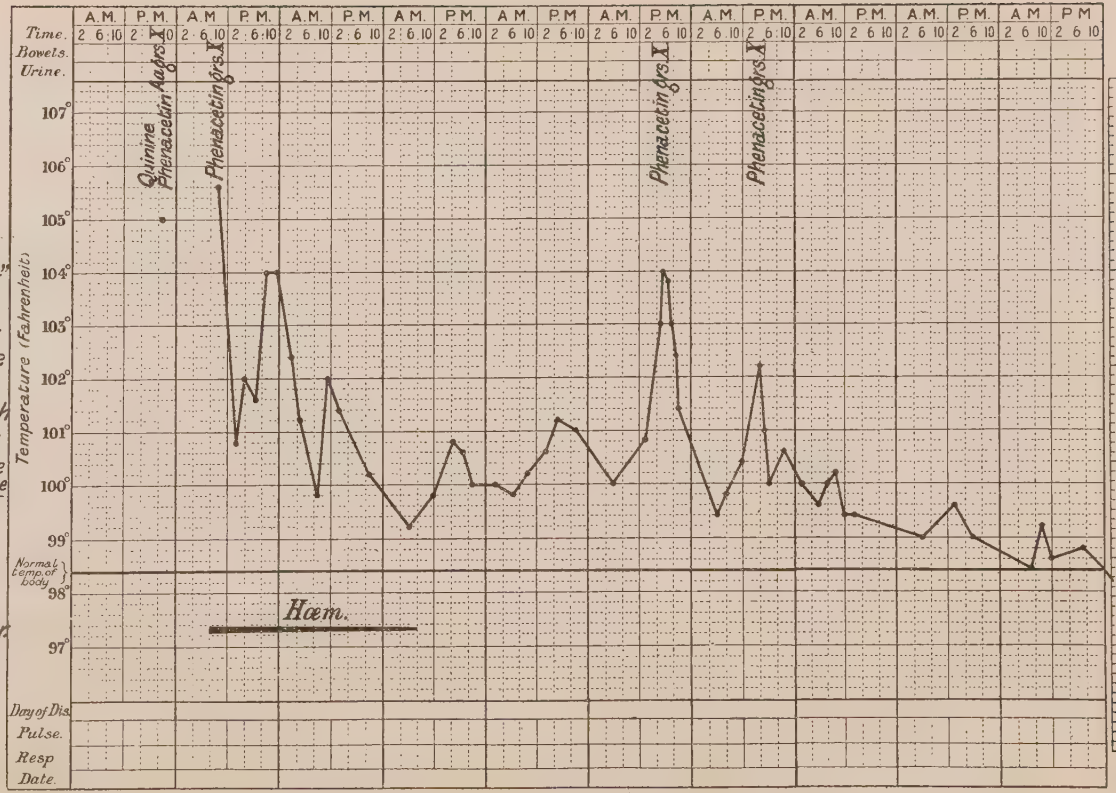


Chart 9.

DISEASE

Blackwater Fever 1st attack.

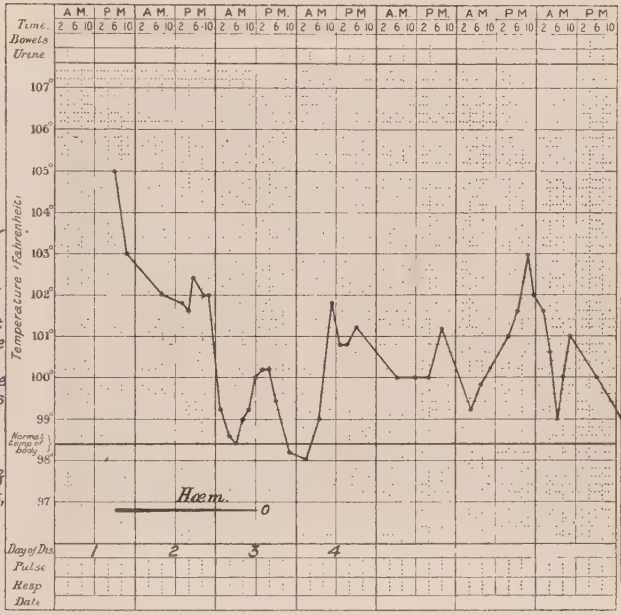
Name S.

Under care of Dr Gray.

NOTES OF CASE

3½ years in B.C.A. Had very little fever after 1st year, been most of the time in Angoni & Shiré Highlands. Not a quinine taker, but took 5 grs. rather more than a week ago. "Fever" the day before the attack, as well as the same day. Initial Rigor. Treatment:- ½ lig. Hydrarg. Perchlor. & Sodm. Bicarb. at first, & then Terebine.

RESULT Recovery.



DISEASE

Blackwater Fever 2nd attack.

Name S.

Under the care of Dr Hearsay.

NOTES OF CASE

Previous attack 4 months ago. Since then has had good health. Fever for 3 hours every day. Last quinine grs. X, 12 hours before attack, & Antipyrine grs. V, 4 hours before. Initial Rigors. Treatment:- Sodm. Bicarb. & Lig. Hydrarg. Perchlor.

RESULT Recovery.

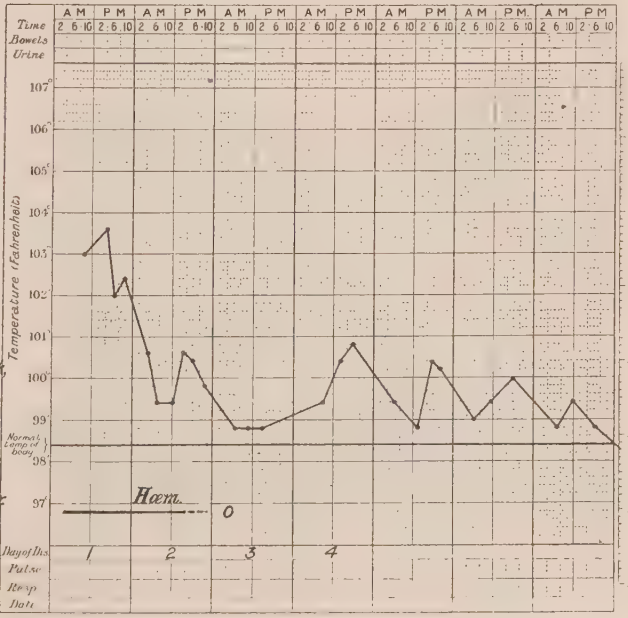


Chart 10.

DISEASE

Blackwater Fever
1st attack.
Hyperpyrexia.
Name R.B.
Under care of
Dr. Mac Vicar.

NOTES OF CASE

Nine years in B.C.A.
Strong, full-blooded man.
Fever for 3 days, but felt better on 2nd day & was able to travel.
In addition to Quinine, digitalis & stimulants freely administered.

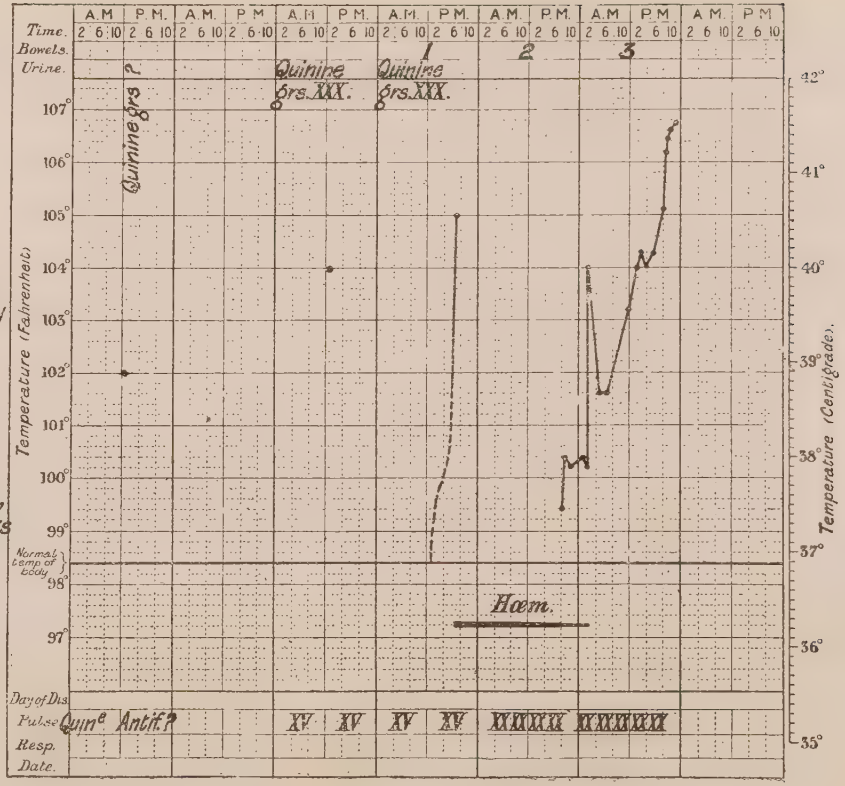


Chart II.

DISEASE

Blackwater Fever
Hyperpyrexia.

Name J.B.

Under care of
M.O. Blantyre Mission.

NOTES OF CASE

Had Blackwater Jan. 3rd & 4th under 48 hrs.
Temperature 104° fell about a degree daily from 5th.
On 10th (M) 99° F.
Rigor in afternoon & again passed Blackwater. Urine cleared in about 24 hours.
Temperature was never normal but fell gradually.
From 14th - 17th was treated with every available antipyretic. Cold bath alone had any success.

RESULT Died.

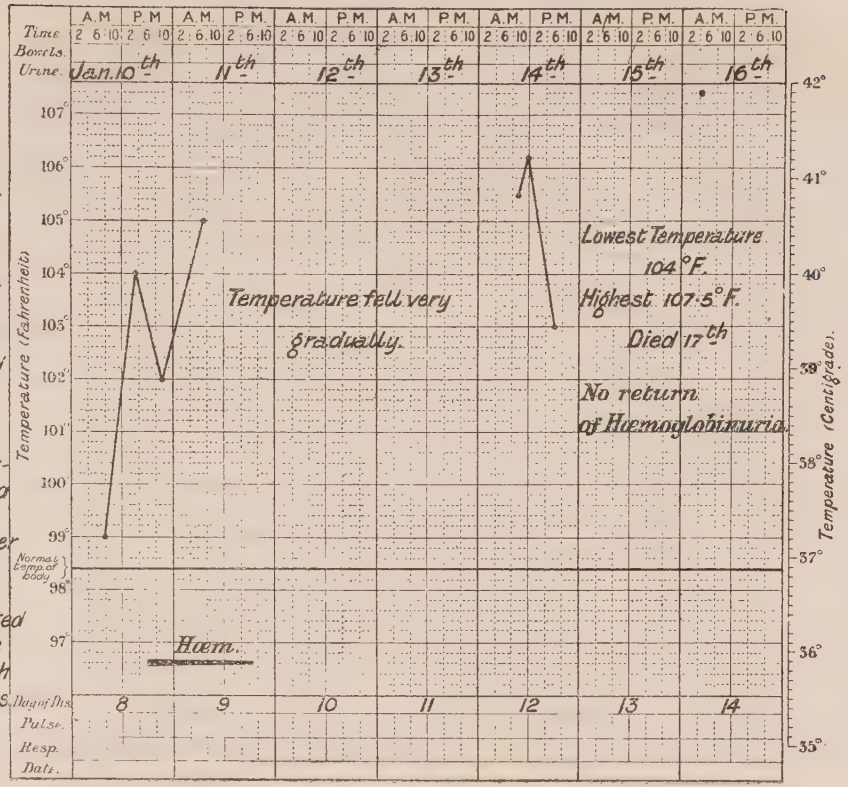


Chart 12.

DISEASE

Blackwater Fever.
Suppression.
Name C.M.
Under the care of
Dr Gray P.M.O.

NOTES OF CASE

Has been in B.C.A. 7 years.
Led an irregular life with much exposure.
Not had very much fever.
Had fever a fortnight ago following exposure.
Since then had several attacks. Was about, but not feeling well the day of the attack.
No quinine for a fortnight, & then only a small dose.
His attacks of fever since then have been untreated.
Terebine Treatment.
Much vomiting. Suppression (incomplete) within 24 hrs. of the onset.
Severe Epistaxis.

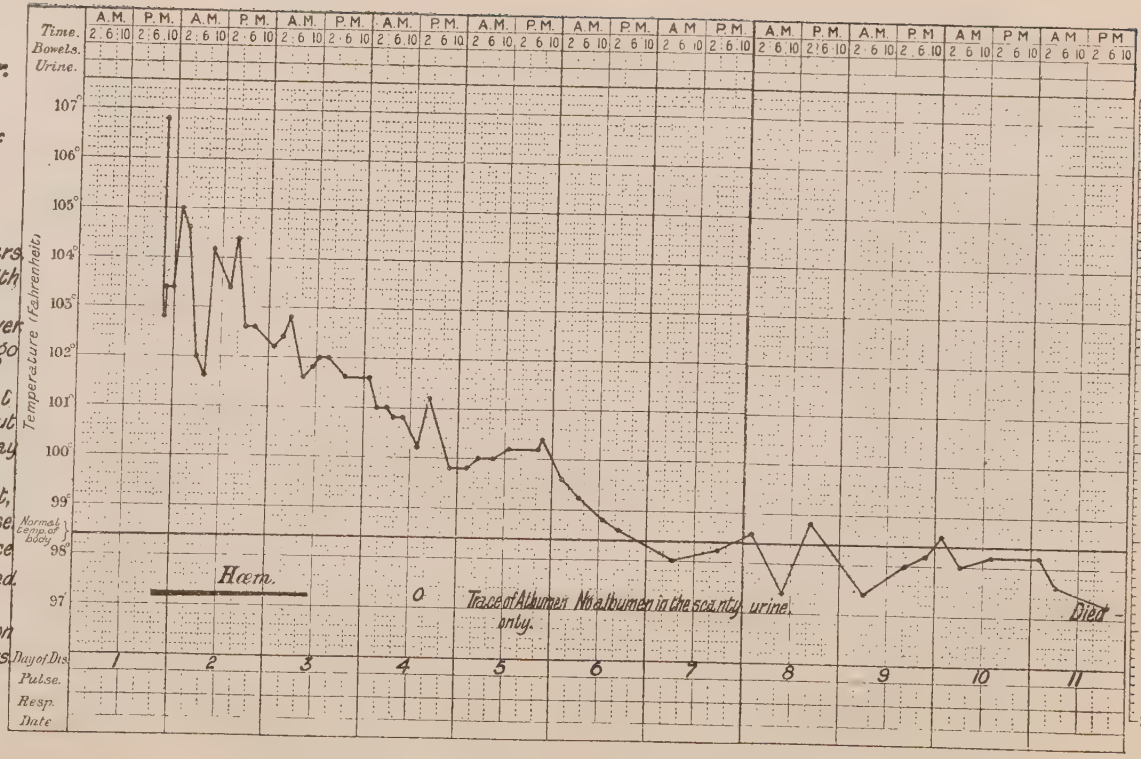


Chart 13.

DISEASE

Blackwater Fever.
Death from Lobar Pneumonia.
Name G
Under the care of
Dr Kerr Cross

NOTES OF CASE

Had been in India & had fever there.
8 months in B.C.A., no definite attacks of fever, but malaise at times.
Had not been feeling well for over a week.
Onset sudden, during sleep, with severe rigor.
Very little vomiting.
Terebine Treatment.
Death from Lobar Pneumonia.

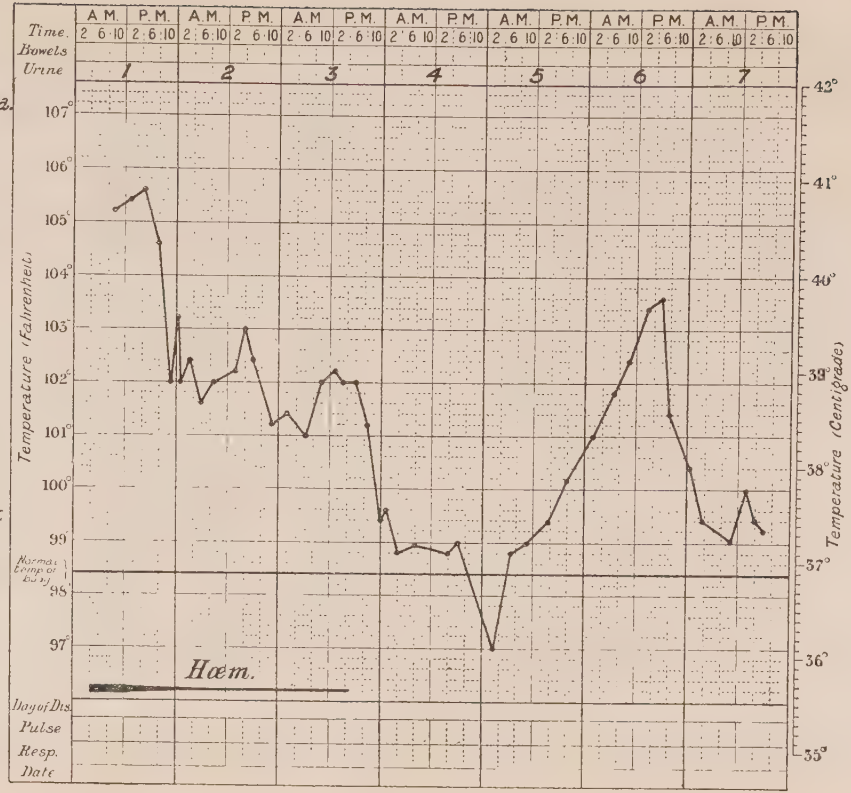


Chart 14.

DISEASE

Blackwater Fever 3rd attack.

Name R.

Under care of Dr Hearsay.

NOTES OF CASE

Previous attacks 18 months & 32 months ago.
Has had much fever.
Parasitic invasions sometimes large.
Day previous to Blackwater was up & about but felt ill in afternoon & went to bed. Took antifebrin & later a large dose of quinine ? 25 grs.
Rigor initial. Vomiting slight.
Urine was clearing rapidly on the 3rd day but again became quite dark in evening.
No parasites found, but pigd leucocytes in films on 3rd day.
Treatment:–
Bicarbonate of Soda, & Liq. Hydrarg. Perchlor.

RESULT Recovery.

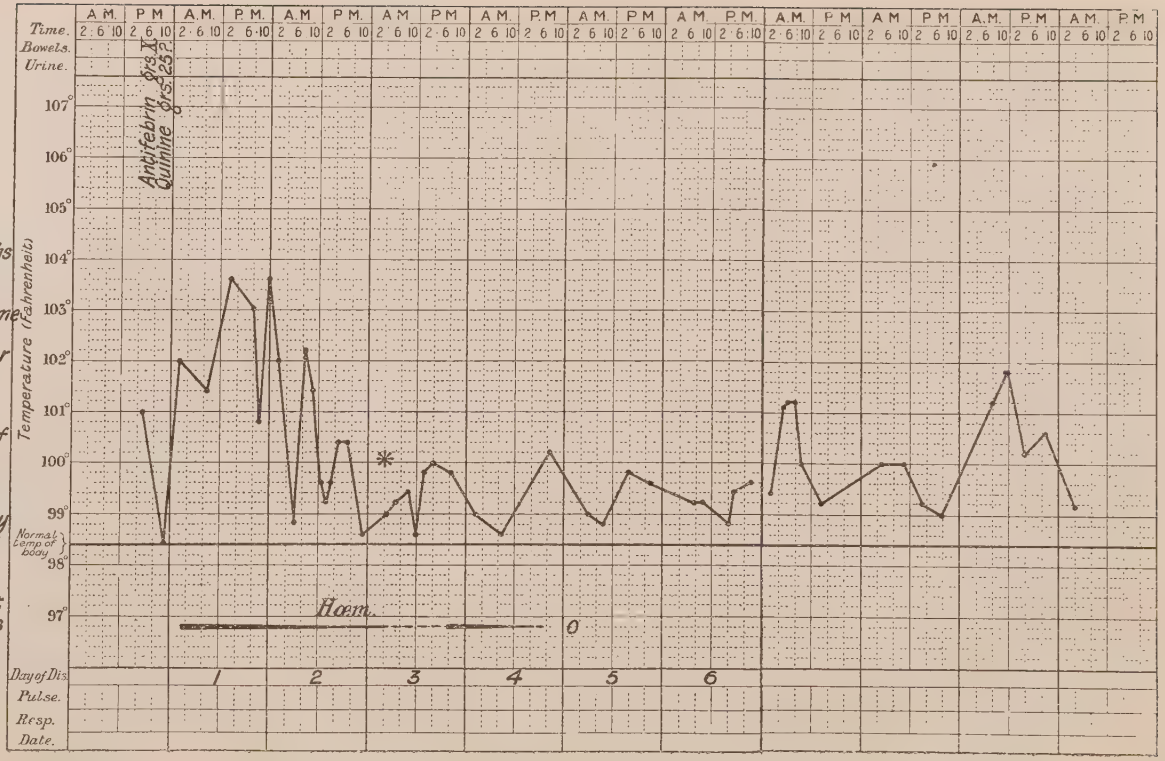
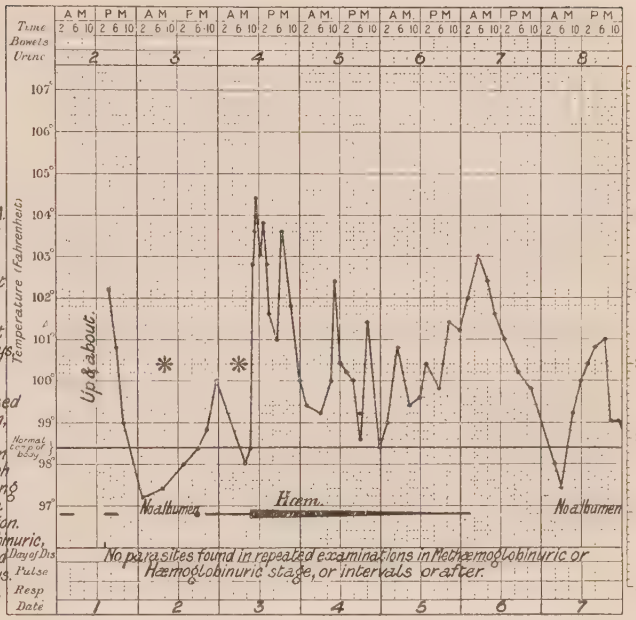
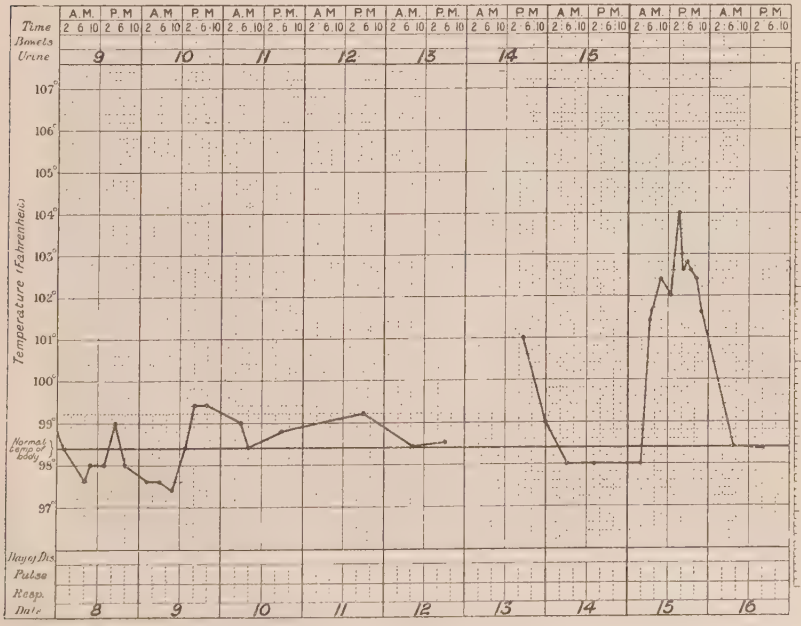


Chart 15.
DISEASE
"Blackwater Fever"
1st attack.
Name H.
Under the care of
Dr Gray P.M.O.

NOTES OF CASE

Been 1 yr. 10 mths. in B.C.A. Had a good deal of fever & at one time took fair doses of Quinine. Of late has taken little, & the last time was 3 or 4 days before onset. Passed "brown" urine in night having had fever for 2 days. Urine clear in morning & he went out but had to return. In afternoon passed "brown" urine, Methæmoglobin, it again cleared. Following afternoon again passed Methæmoglobin which continued till the following morning when there was a sudden change in his condition. Next urine passed Hæmoglobinuric, so dark that it was estimated that it would persist 2½-3 days. Pain Hepatic not Renal.





ILLUSTRATIVE URINE CHARTS.

URINE CHARTS, showing the rate per hour, in ounces, at which the urine is excreted.

A (1) corresponds to Temperature Chart 13.
A (2) corresponds to Temperature Chart 6.
A (3) Temperature Chart similar to 6. Not given.
A (4) corresponds to Temperature Chart 1.

These charts show an increase in the amount during the hæmoglobinuric period, followed by a drop to below normal as the urine clears, and a slow return to normal.

B. (Corresponding to Temperature Chart 8.) Merely slight increase in the rate during the hæmoglobinuric period. No marked drop as the urine cleared.

C. (Corresponding to Temperature Chart 2.) There is a decided fall in the amount passed in the first twenty-four hours; (?) indicating a tendency to early suppression, followed by a great increase in the second twenty-four hours, and a subsequent fall as the urine cleared.

The first fall was not due to *retention* of urine.

D. (Corresponding to Temperature Chart 12.) Suppression case. The amounts passed after the first twenty-four hours are too small to be indicated on this scale.

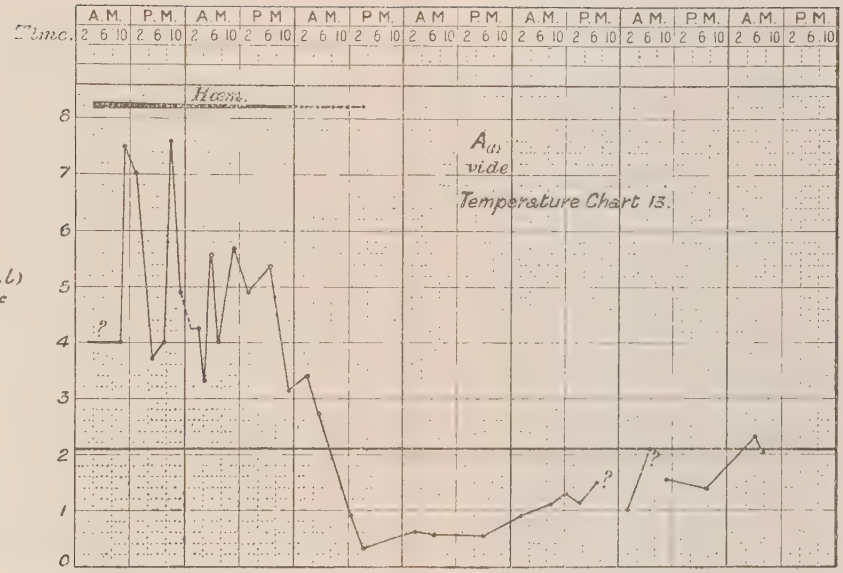
E. (Corresponding to Temperature Chart 15.)

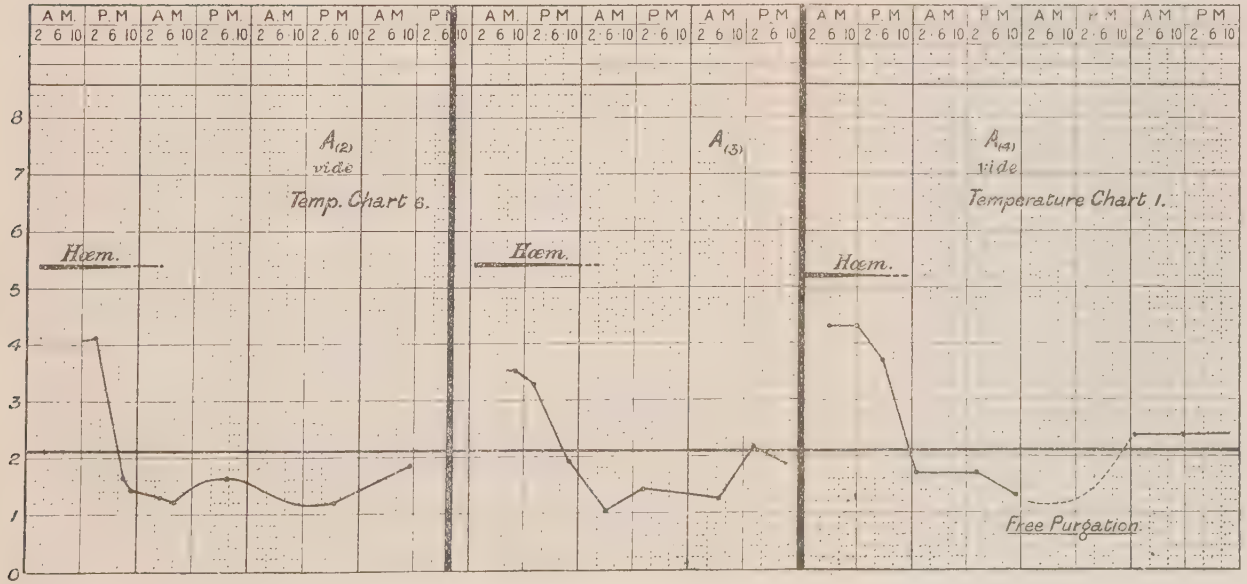
Urine Charts.

Indicating the rate of excretion of Urine in ounces per hour.

The thick line (horizontal) indicates the duration of the Hæmoglobinuria.

A





U

A
A
A
A

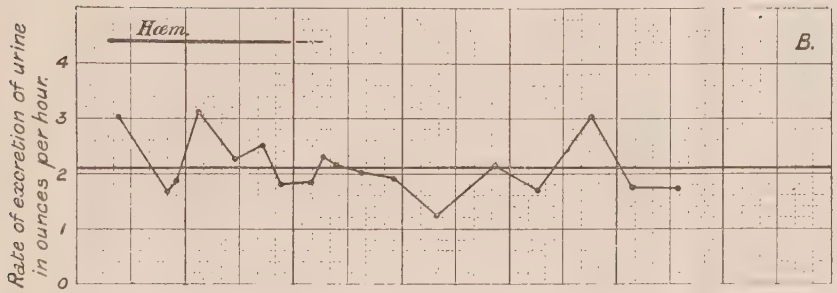
I

C

D

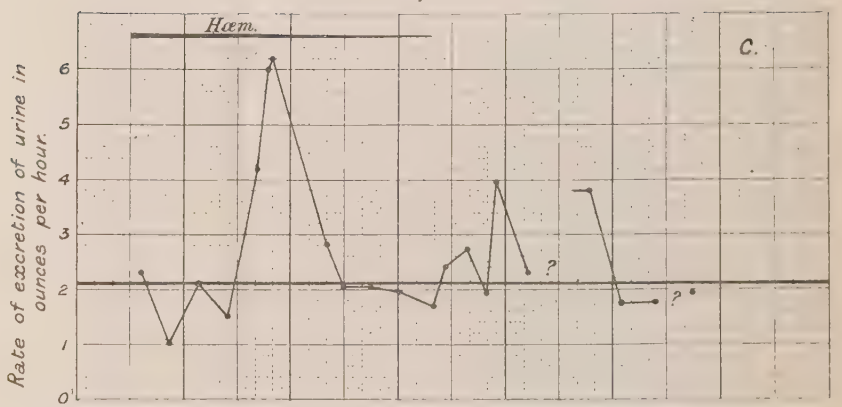
E

B. vide Temperature Chart 8.



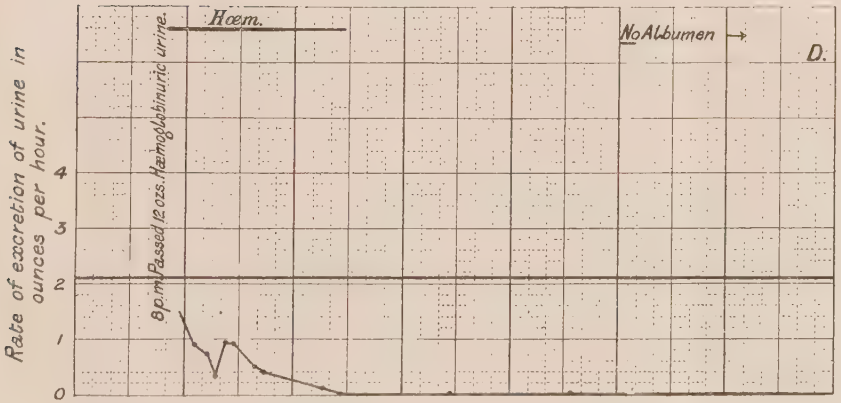
Slight increase in rate of excretion during the Hæmoglobinuric Period.
No marked fall below the normal as the urine cleared.

C. vide Temperature Chart 2.



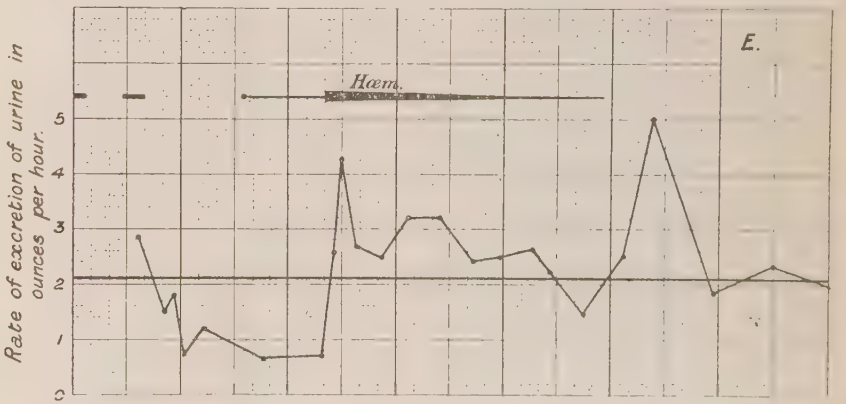
Early fall in the amount of urine excreted. During the time that the rate was low there was very frequent micturition. No retention. Great increase in the amount & rate of excretion followed this period.
No marked fall below normal as the urine cleared.
Subsequent increase in the rate of excretion. From more imperfect notes of other cases I gather that such a subsequent rise is common.

D. vide Temperature Chart 12.



"Suppression Case." Twelve ounces were passed within half an hour of the first symptoms; after that, the rate was always below normal, & after the first 24 hours very little was passed.
The patient died after 10 days.

E. vide Temperature Chart 15.



Previous to the thick horizontal line the urine contained Methæmoglobin at the times corresponding to the thinner horizontal lines.
The rate of excretion at first high, fell as the urine cleared; it did not rise with the onset of Methæmoglobin again, but did with the onset of Hæmoglobinuria.
Slight fall as the urine cleared, followed by a marked subsequent increase.

ERRATA.

REPORTS TO THE MALARIA COMMITTEE, 1899–1900.

(Malarial and Blackwater Fevers of British Central Africa.)

Page 24, line 22. *Omit* "Report I."
,, 26 ,, 29. *For* "plasterer" *read* "planter."
,, ,, lines 41 and 43. *For* "Inpimbe" *read* "Mpimbe."
,, 27, line 2. *Omit* "Case I."
,, 28 ,, 2. *For* "Case II" *read* "Case III"; *omit* "*vide* also Chart X."
,, 30, lines 28 and 37. *For* "Bright's" *read* "Weigert's."
,, 31 ,, 3 and 37. *For* "K_4TeCy_{76}" *read* "K_4FeCy_6."
,, 32, line 13. *For* "narrow" *read* "marrow."
,, 33 ,, 2. *For* "Case III" *read* "Case IV"; *omit* "*vide* also Chart VII."
,, 36 ,, 2. *For* "Case IV" *read* "Case V"; *omit* "*vide* also Chart VIII."
,, 38 ,, 12. *For* "Chart IV" read "Chart VIII."
,, ,, ,, 18, columns 4 and 5. *For* "H" *read* "No."
,, ,, ,, 19 ,, ,, ,, ,,
,, ,, ,, 21 ,, ,, ,, ,,
,, ,, ,, 22 ,, ,, ,, ,,
,, 40 ,, 6. *For* "Case V" *read* "Case II"; *omit* "*vide* also Chart IX."
,, 41 ,, 42. *For* "Chart V" *read* "Chart VI."
,, 62 ,, 41. *For* "Case I" *read* "Case II."
,, 63 ,, 25. *For* "Case II" *read* "Case III."
,, 66 ,, 10. *For* "Case I" *read* "Case II"; *omit* "of our previous report."
,, 69 ,, 13. *For* "Case I" *read* "Case II."
,, ,, ,, 15. *For* "Case III" *read* "Case IV."
,, ,, ,, 22. *For* "Case II" *read* "Case III."

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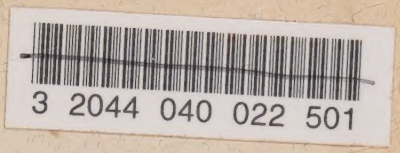

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